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Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) Publication number:

0 525 420 A1

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: **92111129.0**

(22) Date of filing: **01.07.92**

(51) Int. Cl.⁵: **C07D 307/56, C07D 307/84, C07D 307/85, C07D 307/68, C07D 307/38, C07D 307/42, C07D 307/52, C07D 213/32, C07D 235/06, C07D 261/08, C07D 263/20, C07D 277/26, C07D 295/125, C07D 405/12, C07D 407/12, C07D 409/12, C07C 271/54, C07C 317/28, C07C 323/41, C07K 5/06, A61K 31/16, A61K 31/325, A61K 31/34, A61K 31/35, A61K 31/36, A61K 31/38, A61K 31/44**

(30) Priority: **01.07.91 JP 160674/91**
24.10.91 JP 277905/91
25.12.91 JP 343668/91

(43) Date of publication of application:
03.02.93 Bulletin 93/05

(54) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI LU MC NL PT SE

(71) Applicant: **MITSUBISHI KASEI CORPORATION**
5-2, Marunouchi 1-chome Chiyoda-ku
Tokyo(JP)

(72) Inventor: **Ando, Ryoichi**
2-11-3, Ogawa
Machida-shi, Tokyo-to(JP)
Inventor: **Ando, Naoko**
2-11-3, Ogawa
Machida-shi, Tokyo-to(JP)
Inventor: **Masuda, Hirokazu**

2-6-3, Tachibanadal, Midori-ku
Yokohama-shi, Kanagawa-ken(JP)

Inventor: **Morinaka, Yasuhiro**

1-15-2, Kandatsuhigashi

Tsuchiura-shi, Ibaraki-ken(JP)

Inventor: **Takahashi, Chizuko**

34-8-302, Shiratoridai, Midori-ku

Yokohama-shi, Kanagawa-ken(JP)

Inventor: **Tamao, Yoshikuni**

2-5-1, Naruse

Machida-shi, Tokyo-to(JP)

Inventor: **Tobe, Akihiro**

3, Sakuradal, Midori-ku

Yokohama-shi, Kanagawa-ken(JP)

(74) Representative: **Hansen, Bernd, Dr.**
Dipl.-Chem. et al
Hoffmann, Eitle & Partner Patent- und
Rechtsanwälte Arabellastrasse 4 Postfach
81 04 20
W-8000 München 81(DE)

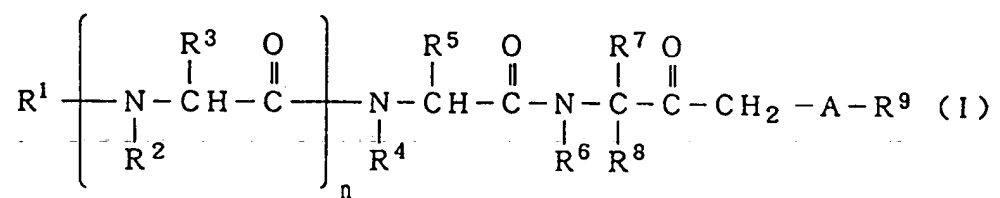
(54) **Pseudopeptides and dipeptides characterised by a substituted methyl ketone moiety at the C-terminus as thiol protease inhibitors.**

(57) **A novel ketone derivative (I) which possesses a potent inhibitory activity against thiol protease such as papain, cathepsin B, cathepsin H, cathepsin L, calpain or the like with excellent properties regarding oral absorbance, tissue transference and cell membrane permeability, and are clinically useful in the treatment of**

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various diseases such as muscular dystrophy, amyotrophy. Also provided are a process for producing the compound (I) and a pharmaceutical composition containing the same.



FIELD OF THE INVENTION

The present invention relates to novel ketone derivatives. More particularly, this invention relates to novel ketone derivatives having a potent inhibitory activity against thiol protease such as papain, cathepsin B, cathepsin H, cathepsin L, calpain or the like.

BACKGROUND OF THE INVENTION

In accordance with the elucidation of the in vivo activity of thiol protease such as papain, cathepsin B, cathepsin H, cathepsin L, calpain or the like, it has been found that their extraordinary hypersthenia causes various diseases. Further, there is increasing the report which shows thiol protease inhibitors are effective on such disease in animal models.

It is considered that thiol protease such as calpain, cathepsin B or the like takes part in the initial process such as disappearance of Z line through the decomposition of muscular fiber protein in the collapse of skeletal muscle as seen in muscular disease such as muscular Dystrophy, amyotrophy or the like [Taisha (Metabolism), 25, 183 (1988)]. Furthermore, E-64-d, namely a thiol protease inhibitor, has been reported to have life-prolonging effect in experimental muscular dystrophy hamster [Journal of Pharmacobio dynamics, 10, 678 (1987)]. Accordingly, such thiol protease inhibitors are expected to be useful as therapeutic agents for the treatment of muscular dystrophy, amyotrophy or the like.

The main cause of the post-ischemic cellular disorder occurs during ischemic diseases such as cardiac infarction, stroke and the like is active oxygen produced by xanthine oxidase. It has been reported that, during the ischemia, the increase in Ca^{2+} concentration results in the activation of calpain which restrictively degrade xanthine dehydrogenase, a precursor of xanthine oxidase, to give xanthine oxidase [New England Journal of Medicine, 312, p.159, (1985)]. It has also been reported that the activation of calpain may directly cause the necrosis of myocardial cells or neurocytes [Saishin Igaku 43, p.783, (1988)]. There have been reported that NCO-700, a calpain inhibitor, is effective on cardiac infarction when tested on animal models [Arzneimittel Forschung/Drug Research, 36, p.190, p.671, (1986)], and that E-64-C inhibits the degradation of microtubule-associated protein after the brain ischemia [Brain Research, 526, p.177, (1990)]. These reports indicate that a calpain inhibitor can be useful for the treatment of ischemic diseases such as cardiac infarction, stroke and the like.

The cause of senile plaque which is found specifically in the brain of patients suffering from Alzheimer's disease is known to be the precipitated amyloid, a protein produced by the decomposition of an amyloid precursor protein (APP). Although APP does not give amyloid as a normal metabolite, it may be converted into amyloid under an abnormal metabolism where protease is extremely activated, and precipitated as senile plaque [Scientific American, (11), p.40, (1991)]. Therefore, protease inhibitor is expected to be useful for the treatment of Alzheimer's disease.

The activation of calpain has been observed in a brain trauma model of rabbit [Neurochemical Research, 16, p.483, (1991)]. It has also been observed, the administration of leupeptin, a calpain inhibitor, can protect axon in brain trauma models of rat [Journal of Neurosurgery, 65, p.92, (1986)]. Thus, calpain inhibitors are considered to be useful for improving the consciousness disturbance or motor disturbance caused by brain trauma.

It has also been reported that myelin-associated protein exists in dendrite of neurocytes is decomposed by calpain [Journal of Neurochemistry, 47, p.1007, (1986)], indicating that calpain inhibitors may be effective on diseases caused by the demyelination of neurocytes such as multiple sclerosis, peripheral nervous neuropathy and the like.

The main cause of the turbidity during cataract is hydrolytic products of a water-soluble protein crystallin by protease in lens. It has been observed the increase in calcium concentration in lens of cataractous animal models and some of human cataract [Investigative Ophthalmology & Visual Science, 28, p.1702, (1987); Experimental Eye Research, 34, p.413, (1982)]. The dominant protease contained in lens is calpain [Lens and Eye Toxicity Research, 6, p.725, (1989)]. These facts indicate that the abnormal sthenia of calpain can be one of the causes of cataract. There is a report that E-64, an inhibitor of calpain, is effective on cataract in animal models [Investigative Ophthalmology & Visual Science, 32, p.533, (1991)], indicating that calpain inhibitors can be useful in the treatment of cataract.

Neutrophils, which is deeply associated to inflammation, show the degranulation or production of superoxides in response to the stimulations by a chemotactic factor or phorbol ester through a mechanism appeared to be mediated by protein kinase C (PKC). Calpain participates in the activation of PKC in the manner where it promotes the degranulation and inhibits the production of superoxides [Journal of Biological Chemistry, 263, p.1915, (1988)]. In another report, the concentration of cathepsin B in macro-

phage in rat is 30 to 40 times that of leukocytes and neutrophils, and the concentration of enzyme in inflammatory macrophage is 6 times that of normal macrophages [Journal of Biochemistry, 98, p.87, (1985)-]. These facts indicate that thiol protease inhibitors are useful as anti-inflammatory drugs.

The type I allergy reaction is mediated by immunoglobulin E (IgE) produced in the subject immunized with an antigen. Estatin A, a thiol protease inhibitor, has been reported to specifically inhibit the production of IgE without affecting on the production of IgG [The Journal of Antibiotics, 42, p.1362, (1989)]. Accordingly, thiol protease inhibitors are considered to be useful as antiallergic drugs.

In case of necrosis of hepatic cells, it is believed that impairment of the cell membrane leads to an increase in the permeability of Ca^{2+} , an increase in intracellular Ca^{2+} concentration, an activation of calpain, and, as the result, the decomposition of its substrate such as skeletal protein takes place, which results in the death of cells. Accordingly, a calpain inhibitor can be used as a therapeutic agent for fulminant hepatitis.

Cathepsins such as cathepsin B and cathepsin L are involved in decomposition of bone collagen in osteoclast. It has been reported that administration of an inhibitor of cathepsins, E-64 or estatins A, to a rat which has an enhanced bone destruction by administration of parathyroid hormone leads to a decrease of calcium concentration and hydroxyproline concentration in blood [Biochemical and Biophysical Research Communication, 125, p.441, (1984); Japanese Patent Publication (kokai) No. 218610/1990]. Accordingly, it is believed that an inhibitor of cathepsins can be a therapeutic agent for osteoporosis, hypercalcemia and the like.

There exist, as a substrate for calpain, sex hormone receptors such as estrogen receptor and androgen receptor, and it is known that calpain activates these receptors. Accordingly, it is considered that an abnormal sthenia of calpain causes a disease which is suspected to be caused by an abnormal activation of the sex hormone receptors, for example, breast carcinoma, prostatic carcinoma or prostatomegaly. It is believed that an inhibitor for calpain can be a therapeutic agent for the above disease.

Receptors for epidermal growth factor (EGF) are also considered to be activated in association with the canceration of cells. It is known that calpain activates the EGF receptors as its substrate. Furthermore, it has been reported that calpain is activated in cells which have been infected with adult T cell human leukocyte virus (ATLV/HTLV-1) [Seikagaku, 57, p.1202, (1985)]. On the other hand, it is said that cathepsin B is greatly involved in a process of cancer metastasis because it accelerates decomposition of collagen which is a important step for the cancer metastasis or directly decomposes collagen, and because it has a profound correlation with plasma membrane of neoplastic cells [Tumor Progression and Markers, p.47, (1982); Journal of Biological Chemistry, 256, p.8536, (1984)]. These facts suggest that a thiol protease inhibitor has an ability to suppress the growth of cancer cells and prevent the metastasis of cancer.

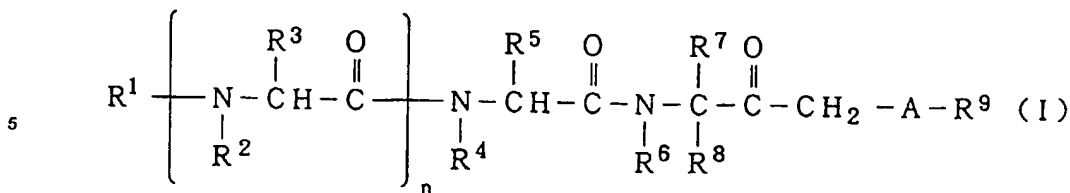
Activation of platelet causes the aggregation thereof which is a cause of thrombus. It has been reported that an inhibitor of calpain, E-64-d, suppressed aggregation of platelet caused by thrombin [Thrombosis Research, 57, p.847, (1990)]. Accordingly, the inhibitor of calpain can be used as an inhibitor against aggregation of platelet.

As described above, an abnormal sthenia of thiol protease causes various diseases and a validity of several thiol protease inhibitors in animal models has been reported. However, most of known inhibitors, for example, epoxy succinate derivatives such as E-64 [Agricultural and Biological Chemistry, 42, p.529, (1978)], E-64-d [Journal of Biochemistry, 93, p.1305, (1983)], NCO-700 [Japanese Patent Publication (kokai) No. 126879/1983], and estatins A and B [The Journal of Antibiotics, 42, p.1362, (1989)], or α -substituted ketone of a peptide such as chloromethyl ketone [Journal of Biochemistry, 99, p.173, (1986)] and acyloxymethyl ketone [Biochemistry, 30, p.4678, (1991)] are irreversible inhibitors. It is generally said that the irreversible inhibitors are highly toxic because they are liable to react with non-specifically to components consisting living body, other than target enzymes. Therefore, there have been few compounds applicable to clinical use so far. Although peptidyl aldehydes such as leupeptin [The Journal of Antibiotics, 22, p.183, (1969)] or calpeptin [Journal of Enzyme Inhibition, 3, p.195, (1990)] are known as reversible inhibitors, they also have problems in chemical and in vivo stabilities, cell membrane permeabilities and the like.

SUMMARY OF THE INVENTION

The present inventors investigated into various compounds with aim of developing reversible inhibitors against thiol protease, which have excellent properties concerning absorbance on oral administration, tissue distribution and cell membrane permeability, and have found that certain derivatives of ketone have such desired properties.

Thus, the present invention provides ketone derivatives of the general formula (I):



wherein R¹ is hydrogen atom, R¹⁰-CO-, R¹⁰-O-CO-, R¹⁰-SO₂- or R¹⁰-NH-CO- (in which R¹⁰ is C₁ - C₂₀ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, C₃ - C₁₅ cycloalkenyl group, optionally substituted C₆ - C₁₄ aryl group, optionally substituted and partially hydrogenated C₁₀ - C₁₄ aryl group, fluorenyl group, optionally substituted heterocyclic group, C₃ - C₁₅ cycloalkyloxy group, optionally substituted C₆ - C₁₄ aryloxy group, optionally substituted and partially hydrogenated C₆ - C₁₄ aryloxy group, optionally substituted heterocyclic oxy group, optionally substituted C₇ - C₂₀ aralkyloxy group and optionally substituted C₆ - C₁₄ arylthio group; C₃ - C₁₅ cycloalkyl group; optionally substituted C₆ - C₁₄ aryl group; optionally substituted and partially hydrogenated C₆ - C₁₄ aryl group; optionally substituted C₂ - C₁₀ alkenyl group; or optionally substituted heterocyclic group);

R², R⁴ and R⁶ each are independently hydrogen atom or C₁ - C₅ alkyl group;

R³ and R⁵ each are independently hydrogen atom, C₇ - C₂₀ aralkyloxy group, optionally substituted C₆ - C₁₄ aryl group, C₁ - C₁₀ alkoxy group or optionally substituted C₁ - C₂₀ alkyl group; or

R² and R³ and/or R⁴ and R⁵ taken together may form an optionally substituted nitrogen-containing heterocyclic ring;

R⁷ is C₁ - C₂₀ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, hydroxyl group, C₁ - C₅ alkoxy group optionally substituted by heterocyclic group, C₆ - C₁₄ aryloxy group, C₇ - C₂₀ aralkyloxy group, C₁ - C₅ alkylthio group optionally substituted by heterocyclic group, C₆ - C₁₄ arylthio group, C₇ - C₂₀ aralkylthio group, carboxyl group, carbamoyl group, C₂ - C₆ alkoxycarbonyl group, heterocyclic group and optionally substituted C₆ - C₁₄ aryl group; hydrogen atom; C₇ - C₂₀ aralkyloxy group; optionally substituted C₆ - C₁₄ aryl group or C₁ - C₁₀ alkoxy group;

R⁸ is hydrogen atom, C₁ - C₅ alkyl group or optionally substituted C₇ - C₂₀ aralkyl group; or

R⁷ and R⁸ taken together may form optionally substituted benzyldene group or C₃ - C₁₅ cycloalkyl group;

A is -S-, -SO-, -SO₂-, -O- or -N(R¹¹)- (in which R¹¹ is hydrogen atom or optionally substituted C₁ - C₂₀ alkyl group), and

(1) when A is -S-, -SO- or SO₂-, then R⁹ is optionally substituted C₆ - C₁₄ aryl group or -(CH₂)_m-X (in which X is hydrogen atom, hydroxyl group, C₁ - C₅ alkylthio group, C₂ - C₆ alkoxycarbonylamino group, optionally substituted heterocyclic group, amino group, C₁ - C₅ monoalkylamino group, C₂ - C₁₀ dialkylamino group, C₂ - C₆ acylamino group, halogen atom, C₁ - C₅ alkoxy group, optionally substituted C₆ - C₁₄ aryl group or optionally substituted C₆ - C₁₄ aryloxy group; and m is 0 or an integer of 1 to 15); provided that if R¹ is benzyloxycarbonyl group, R⁴, R⁶ and R⁸ all are hydrogen atom, R⁵ is benzyl group, R⁷ is methyl group and n is 0, then -A-R⁹ is not methylthio group;

(2) when A is -O-, then R⁹ is hydrogen atom or -(CH₂)_l-X (in which l is an integer of 1 to 15; and X is as defined above); or

(3) when A is -N(R¹¹)-, then R⁹ is optionally substituted C₆ - C₁₄ aryl group or -(CH₂)_m-X (in which X and m are as defined above); or R⁹ and R¹¹ taken together may form an optionally substituted nitrogen-containing heterocyclic ring; and

n is 0 or 1, or pharmaceutically acceptable salts thereof.

The present invention also provides a pharmaceutical composition containing, as an active ingredient, a ketone derivative of the above formula (I) or a salt thereof.

The present invention also provides a process for the preparation of ketone derivatives of the above formula (I) or salts thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

Figs. 1, 2 and 3 show abilities of the compounds according to the present invention (compounds of Examples 3, 113 and 190, respectively) to reversibly inhibit calpain.

DETAILED DESCRIPTION OF THE INVENTION

Definition:

5 For the purpose of the invention the following terms used herein are defined as follows:

In the above formula (I), $C_1 - C_{20}$ alkyl group in the definition of R^{10} includes methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, tert-pentyl group, hexyl group, isohexyl group, heptyl group, octyl group, nonyl group, decyl group, undecyl group, dodecyl group, tridecyl group, tetradecyl group, pentadecyl group, hexadecyl group, heptadecyl group, octadecyl group, nonadecyl group, icosyl group and the like. Such alkyl group may be optionally substituted by one or more substituents selected from the group consisting of $C_3 - C_{15}$ cycloalkyl group such as cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group, cyclononyl group, cyclodecyl group, cycloundecyl group, cyclododecyl group, cyclotridecyl group, cyclotetradecyl group, cyclopentadecyl group or the like; $C_3 - C_{15}$ cycloalkenyl group such as cyclopropenyl group, cyclobutenyl group, cyclopentenyl group, cyclohexenyl group, 1,4-cyclohexadienyl group, cycloheptenyl group, cyclooctenyl group, cyclodecenyl group, cyclododecenyl group, cyclotetradecenyl group or the like; $C_6 - C_{14}$ aryl group such as phenyl group, 1-naphthyl group, 2-naphthyl group, anthryl or the like; partially hydrogenated $C_{10} - C_{14}$ aryl group such as 1,2-dihydronaphthyl group, 1,2,3,4-tetrahydronaphthyl group or the like; fluorenyl group; heterocyclic group having 5 to 10 of total ring atom number and containing 1 to 4 hetero atoms selected from oxygen atom, sulfur atom and nitrogen atom to form a ring such as furan ring, dihydrofuran ring, tetrahydrofuran ring, pyran ring, dihydropyran ring, tetrahydropyran ring, benzofuran ring, isobenzofuran ring, chromene ring, chroman ring, isochroman ring, thiophene ring, benzothiophene ring, pyrrole ring, pyrroline ring, pyrrolidine ring, imidazole ring, imidazoline ring, imidazolidine ring, pyrazole ring, pyrazoline ring, pyrazolidine ring, triazole ring, tetrazole ring, pyridine ring, pyridine oxide ring, piperidine ring, pyrazine ring, piperazine ring, pyrimidine ring, pyridazine ring, indolidine ring, indole ring, indoline ring, isoindole ring, isoindoline ring, indazole ring, benzoimidazole ring, purine ring, quinolidine ring, quinoline ring, phthalazine ring, naphthylidine ring, quinoxaline ring, quinazoline ring, cinnoline ring, pteridine ring, oxazole ring, oxazolidine ring, isoxazole ring, isoxazolidine ring, thiazole ring, thiazolidine ring, isothiazole ring, isothiazolidine ring, dioxane ring, dithian ring, morpholine ring, thiomorpholine ring or the like; $C_3 - C_{15}$ cycloalkyloxy group such as cyclopropyloxy group, cyclobutyloxy group, cyclopentyloxy group, cyclohexyloxy group, cycloheptyloxy group, cyclooctyloxy group, cyclodecyloxy group, cyclododecyloxy group, cyclopentadecyloxy group or the like; $C_6 - C_{14}$ aryloxy group such as phenoxy group, 1-naphthyloxy group, 2-naphthyloxy group or the like; partially hydrogenated $C_6 - C_{14}$ aryloxy group such as 1,2,3,4-tetrahydro-1-naphthyloxy group, 1,2,3,4-tetrahydro-2-naphthyloxy group, 5,6,7,8-tetrahydro-1-naphthyloxy group, 5,6,7,8-tetrahydro-2-naphthyloxy group or the like; heterocyclic oxy group having 5 to 10 of total ring atom number and containing 1 to 4 hetero atoms selected from oxygen atom, sulfur atom and nitrogen atom to form a ring such as 2-tetrahydrofuryloxy group, 3-tetrahydrofuryloxy group, 2-tetrahydropyranyloxy group, 3-tetrahydropyranyloxy group, 3-pyrrolyloxy group, 1-piperazinyloxy group, 3-morpholinylloxy group, 4-morpholinylloxy group, 2-pyridyloxy group, 3-pyridyloxy group, 4-pyridyloxy group or the like; $C_7 - C_{20}$ aralkyloxy group such as benzyloxy group, 1-phenylethoxy group, 2-phenylethoxy group, 1-phenylpropoxy group, 2-phenylpropoxy group, 3-phenylpropoxy group, 4-phenylbutoxy group, 5-phenylpentyloxy group, 1-naphthylmethoxy group, 2-naphthylmethoxy group, 1-(1-naphthyl)ethoxy group, 2-(1-naphthyl)ethoxy group, 1-(2-naphthyl)ethoxy group, 2-(2-naphthyl)ethoxy group or the like; and $C_6 - C_{14}$ arylthio group such as phenylthio group, 1-naphthylthio group, 2-naphthylthio group or the like. Examples of $C_3 - C_{15}$ cycloalkyl group, $C_6 - C_{14}$ aryl group, partially hydrogenated $C_{10} - C_{14}$ aryl group and heterocyclic group in the definition of R^{10} are the same as illustrated above for the substituents of $C_1 - C_{20}$ alkyl group. $C_2 - C_{10}$ alkenyl group includes vinyl group, 1-propenyl group, allyl group, isopropenyl group, 1-butenyl group, 2-butenyl group, 2-pentenyl group, 2-hexenyl group, 2-heptenyl group, 2-octenyl group, 2-nonenyl group, 2-decenyl group and the like. Such alkenyl group may be optionally substituted by one or more substituents selected from the group consisting of the above-mentioned $C_3 - C_{15}$ cycloalkyl group, optionally substituted $C_6 - C_{14}$ aryl group, optionally substituted heterocyclic group, $C_3 - C_{15}$ cycloalkyloxy group, optionally substituted $C_6 - C_{14}$ aryloxy group, optionally substituted heterocyclic oxy group, optionally substituted $C_7 - C_{20}$ aralkyloxy group and optionally substituted $C_6 - C_{14}$ arylthio group.

55 Examples of $C_1 - C_5$ alkyl group in the definition of R^2 , R^4 and R^6 are methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, tert-pentyl group and the like.

Examples of optionally substituted $C_1 - C_{20}$ alkyl group in the definition of R^3 and R^5 are the same as

illustrated above for $C_1 - C_{20}$ alkyl group of R^{10} . Such alkyl group may be optionally substituted by one or more substituents selected from the group consisting of halogen atom such as fluorine atom, chlorine atom, bromine atom or the like; $C_3 - C_{15}$ cycloalkyl group as defined in R^{10} ; hydroxyl group; $C_1 - C_5$ alkoxy group such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, sec-butoxy group, tert-butoxy group, pentyloxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group or the like, which may be optionally substituted by heterocyclic group as defined in R^{10} ; $C_6 - C_{14}$ aryloxy group as defined in R^{10} ; $C_7 - C_{20}$ aralkyloxy group as defined in R^{10} ; mercapto group; $C_1 - C_5$ alkylthio group such as methylthio group, ethylthio group, propylthio group, isopropylthio group, butylthio group, isobutylthio group, tert-butylthio group, pentylthio group, isopentylthio group or the like, which may be optionally substituted by heterocyclic group as defined in R^{10} ; $C_6 - C_{14}$ arylthio group as defined in R^{10} ; $C_7 - C_{20}$ aralkylthio group such as benzylthio group, 1-phenylethylthio group, 2-phenylethylthio group, 1-naphthylmethylthio group, 2-naphthylmethylthio group and the like; carboxyl group; carbamoyl group; $C_2 - C_6$ alkoxycarbonyl group such as methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, butoxycarbonyl group, isobutoxycarbonyl group, tert-butoxycarbonyl group, pentyloxycarbonyl group, isopentyloxycarbonyl group or the like; heterocyclic group as defined in R^{10} ; amino group; $C_1 - C_5$ monoalkylamino group such as methylamino group, ethylamino group, propylamino group, isopropylamino group or the like; $C_2 - C_{10}$ dialkylamino group such as dimethylamino group, ethylmethylamino group, diethylamino group or the like; $C_2 - C_6$ alkoxycarbonylamino group such as methoxycarbonylamino group, ethoxycarbonylamino group, propoxycarbonylamino group, isopropoxycarbonylamino group, butoxycarbonylamino group, isobutoxycarbonylamino group, tert-butoxycarbonylamino group, pentyloxycarbonylamino group, isopentyloxycarbonylamino group or the like; $C_2 - C_6$ acylamino group such as acetylamino group, propionylamino group, butyrylamino group, isobutyrylamino group, valerylamino group, isovalerylamino group or the like; guanidino group; oxo group; and $C_6 - C_{14}$ aryl group such as phenyl group, 1-naphthyl group, 2-naphthyl group, anthryl or the like. Examples of $C_7 - C_{20}$ aralkyloxy group and $C_6 - C_{14}$ aryl group are the same as defined in R^{10} and examples of $C_1 - C_{10}$ alkoxy group are methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, sec-butoxy group, tert-butoxy group, pentyloxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group, hexyloxy group, isohexyloxy group, heptyloxy group, octyloxy group, decyloxy group and the like.

Examples of nitrogen-containing heterocyclic ring formed together with R^2 and R^3 as well as R^4 and R^5 are heterocyclic ring having 5 to 10 of total ring atom number and containing 1 to 4 hetero atoms to form a ring such as pyrrolidine ring, piperidine ring, 1,2,3,4-tetrahydroquinoline ring, 1,2,3,4-tetrahydroisoquinoline ring, perhydroquinoline ring, perhydroisoquinoline ring or the like. Such heterocyclic ring may be optionally substituted.

Examples of $C_7 - C_{20}$ aralkyloxy group and $C_6 - C_{14}$ aryl group as defined in R^7 are the same as defined in R^{10} , and examples of $C_1 - C_{10}$ alkoxy group as defined there are the same as defined in R^3 and R^5 . Examples of optionally substituted $C_1 - C_{20}$ alkyl group as defined in R^1 are the same as defined in R^{10} . Such alkyl group may be optionally substituted by one or more substituents selected from the group consisting of $C_3 - C_{15}$ cycloalkyl group as defined in R^{10} ; hydroxyl group; $C_1 - C_5$ alkoxy group such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, sec-butoxy group, tert-butoxy group, pentyloxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group or the like, which may be optionally substituted by heterocyclic group as defined in R^{10} ; $C_6 - C_{14}$ aryloxy group as defined in R^{10} ; $C_7 - C_{20}$ aralkyloxy group as defined in R^{10} ; $C_1 - C_5$ alkylthio group such as methylthio group, ethylthio group, propylthio group, isopropylthio group, butylthio group, isobutylthio group, tert-butylthio group, pentylthio group, isopentylthio group or the like, which may be optionally substituted by heterocyclic group as defined in R^{10} ; $C_6 - C_{14}$ arylthio group as defined in R^{10} ; $C_7 - C_{20}$ aralkylthio group such as benzylthio group, 1-phenylethylthio group, 2-phenylethylthio group, 1-naphthylmethylthio group, 2-naphthylmethylthio group and the like; carboxyl group; carbamoyl group; $C_2 - C_6$ alkoxycarbonyl group such as methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, butoxycarbonyl group, isobutoxycarbonyl group, tert-butoxycarbonyl group, pentyloxycarbonyl group, isopentyloxycarbonyl group or the like; heterocyclic group as defined in R^{10} ; and $C_6 - C_{14}$ aryl group such as phenyl group, 1-naphthyl group, 2-naphthyl group, anthryl or the like.

Examples of $C_1 - C_5$ alkyl group as defined in R^8 are the same as defined in R^2 , R_4 and R_6 . Examples of $C_7 - C_{20}$ aralkyl group are benzyl group, 1-phenethyl group, 2-phenethyl group, 1-phenylpropyl group, 2-phenylpropyl group, 3-phenylpropyl group, 4-phenylbutyl group, 5-phenylpentyl group, 1-naphthylmethyl group, 2-naphthylmethyl group, 1-(1-naphthyl)ethyl group, 1-(2-naphthyl)ethyl group, 2-(1-naphthyl)ethyl group, 2-(2-naphthyl)ethyl group and the like.

Examples of $C_3 - C_{15}$ cycloalkyl group formed together with R^7 and R^8 are the same as defined in R^{10} .

Examples of C₆ - C₁₄ aryl group as defined in R⁹ are the same as defined in R¹⁰.

Examples of C₁ - C₅ alkylthio group, C₂ - C₆ alkoxy-carbonylamino group, C₁ - C₅ monoalkylamino group, C₂ - C₁₀ dialkylamino group, C₂ - C₆ acylamino group and C₁ - C₅ alkoxy group in the definition of X are the same as defined in R³ and R⁵ as the substituents for C₁ - C₂₀ alkyl group, and examples of

5 heterocyclic group, C₆ - C₁₄ aryl group and C₆ - C₁₄ aryloxy group are the same as defined in R¹⁰.
Examples of C₁ - C₂₀ alkyl group in the definition of R¹¹ are the same as defined in R¹⁰, and such alkyl group may be optionally substituted by one or more substituents selected from the group consisting of hydroxyl group; mercapto group; amino group; C₇ - C₂₀ aralkylthio group such as benzylthio group, 1-phenylethylthio group, 2-phenylethylthio group, 1-naphthylmethylthio group, 2-naphthylmethylthio group and the like; C₁ - C₅ alkoxy group, C₁ - C₅ alkylthio group, C₁ - C₅ monoalkylamino group and C₂ - C₁₀ dialkylamino group each of which is the same as defined in R³ or R⁵ as the substituents for C₁ - C₂₀ alkyl group; C₆ - C₁₄ aryloxy group, C₇ - C₂₀ aralkyloxy group, C₆ - C₁₄ arylthio group and heterocyclic group each of which is the same as defined in R¹⁰.

Examples of nitrogen-containing heterocyclic ring formed together with R⁹ and R¹¹ are heterocyclic ring 15 having 5 to 10 of total ring atom number and containing 1 to 4 hetero atoms to form a ring such as pyrrolidine ring, piperidine ring, piperazine ring, 1,2,3,4-tetrahydroquinoline ring, 1,2,3,4-tetrahydroisoquinoline ring, perhydroquinoline ring, perhydroisoquinoline ring or the like. Such heterocyclic ring may be optionally substituted.

In the above definition, aryl group, partially hydrogenated aryl group and heterocyclic group positioned 20 at the terminal of each substituent may be optionally substituted by one or more substituents selected from the group consisting of halogen atom such as fluorine atom, chlorine atom, bromine atom or the like; C₁ - C₅ alkyl group such as methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group or the like; trifluoromethyl group; C₁ - C₅ alkoxy group such as methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, tert-butoxy group, pentyloxy group, isopentyloxy group or the like; C₁ - C₅ cyclic acetal group such as methylenedioxy group, ethylenedioxy group, propylenedioxy group, butylenedioxy group or the like; hydroxyl group; C₂ - C₆ acyloxy group such as acetoxy group, propionyloxy group, butyryloxy group, valeryloxy group or the like; carboxyl group; C₂ - C₆ alkoxy-carbonyl group such as methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, butoxycarbonyl group, isobutoxycarbonyl group, tert-butoxycarbonyl group, pentyloxycarbonyl group or the like; oxo group; C₂ - C₆ acyl group such as acetyl group, propionyl group, butyryl group, valeryl group or the like; amino group; C₁ - C₅ monoalkylamino group such as methylamino group, ethylamino group, propylamino group, isopropylamino group, butylamino group, isobutylamino group, tert-butylamino group, pentylamino group, isopentylamino group or the like; C₂ - C₁₀ dialkylamino group such as dimethylamino group, ethylmethylamino group, diethylamino group, methylpropylamino group, diisopropylamino group or the like; C₂ - C₆ acylamino group such as acetylamino group, propionylamino group, isopropionylamino group, butyrylamino group, isobutyrylamino group, valerylamino group or the like; carbamoyl group; C₂ - C₆ alkylcarbamoyl group such as methylcarbamoyl group, ethylcarbamoyl group, propylcarbamoyl group, isopropylcarbamoyl group, butylcarbamoyl group, tert-butylcarbamoyl group, pentylicarbamoyl group or the like; and C₆ - C₁₄ aryl group such as phenyl group, 1-naphthyl group, 2-naphthyl group, anthryl or the like.

The compounds of the above formula (I) wherein A is -S-, -SO-, -SO₂- or -N(R¹¹)- (in which R¹¹ is optionally substituted C₁ - C₁₅ alkyl group) are preferred in the present invention.

More preferred are the compounds wherein R⁹ is - (CH₂)_m-X (in which X is hydroxyl group, C₁ - C₅ alkylthio group, C₂ - C₆ alkoxy-carbonylamino group, optionally substituted heterocyclic group, amino group, C₁ - C₅ monoalkylamino group, C₂ - C₁₀ dialkylamino group, C₂ - C₆ acylamino group, halogen atom, C₁ - C₅ alkoxy group, optionally substituted C₆ - C₁₄ aryl group or optionally substituted C₆ - C₁₄ aryloxy group; 45 and m is an integer of 1 to 10).

Particularly preferred are the compounds wherein R¹ is hydrogen atom, R¹⁰-CO-, R¹⁰-O-CO-, R¹⁰-SO₂- or R¹⁰-NH-CO- (in which R¹⁰ is C₁ - C₁₅ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, C₃ - C₁₅ cycloalkenyl group, optionally substituted C₆ - C₁₄ aryl group, optionally substituted and partially hydrogenated C₁₀ - C₁₄ aryl group, optionally substituted heterocyclic group, C₃ - C₁₅ cycloalkyloxy group, optionally substituted C₆ - C₁₄ aryloxy group, optionally substituted and partially hydrogenated C₆ - C₁₄ aryloxy group, optionally substituted heterocyclic oxy group, optionally substituted C₇ - C₂₀ aralkyloxy group and optionally substituted C₆ - C₁₄ arylthio group; C₃ - C₁₅ cycloalkyl group; optionally substituted C₆ - C₁₄ aryl group; optionally substituted and partially hydrogenated C₆ - C₁₄ aryl group; optionally substituted C₂ - C₁₀ alkenyl group; or optionally substituted heterocyclic group); R⁴ and R⁵ each is independently hydrogen atom or C₁ 55

- C₅ alkyl group; R⁵ is hydrogen atom, optionally substituted C₆ - C₁₄ aryl group, C₁ - C₁₀ alkoxy group or optionally substituted C₁ - C₁₅ alkyl group; R⁷ is C₁ - C₁₅ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, hydroxyl group, C₁ - C₅ alkoxy group optionally substituted by heterocyclic group, C₆ - C₁₄ aryloxy group, C₇ - C₂₀ aralkyloxy group, C₁ - C₅ alkylthio group optionally substituted by heterocyclic group, C₆ - C₁₄ arylthio group, C₇ - C₂₀ aralkylthio group, carboxyl group, carbamoyl group, C₂ - C₆ alkoxy carbonyl group and heterocyclic group; hydrogen atom; optionally substituted C₆ - C₁₄ aryl group or C₁ - C₁₀ alkoxy group; R⁸ is hydrogen atom.

The ketone derivatives of the general formula (I) above in the present invention can form pharmaceutically acceptable salts thereof. Examples of such salts include, if an acidic group is present, metal salts such as lithium salt, sodium salt, potassium salt, magnesium salt, calcium salt or the like and ammonium salts such as ammonium salt, methylammonium salt, dimethylammonium salt, trimethylammonium salt, dicyclohexylammonium salt or the like and, if a basic group is present, mineral acid salts such as hydrochloride, hydrobromide, sulfate, nitrate or the like and organic acid salts such as methanesulfonate, benzenesulfonate, p-toluenesulfonate, acetate, propionate, tartrate, fumarate, maleate, malate, oxalate, succinate, citrate, benzoate, mandelate, cinnamate, lactate or the like.

Regarding the stereochemistry of double bond regions existing on the ketone derivatives of the general formula (I) above, (E) form, (Z) form and (EZ) form can be provided. As for the stereochemistry of asymmetric carbon, (R) form, (S) form and (RS) form can be given.

Illustrative examples of the ketone derivatives of the general formula (I) above include the compounds as shown in the following Table 1 (in case of n=0) and the compounds as shown in the following Table 2 (in case of n=1).

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Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6		H	-CH ₂ CH(CH ₃) ₂	H	H	H	
7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	H	-S-CH ₃
8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	H	
9		H		H	-CH ₃	H	
10		H		H	-CH ₃	H	

Table 1 (n=0) (continued)


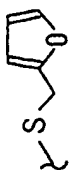
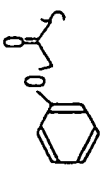

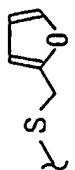
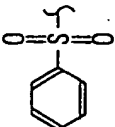

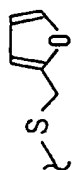
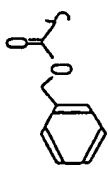

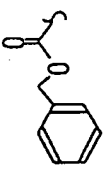
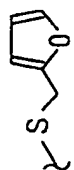
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 1	H	H		H	-CH ₃	H	
1 2		H		H	-CH ₃	H	
1 3		H		H	-CH ₃	H	
1 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
1 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	

Table 1 (n=0) (continued)

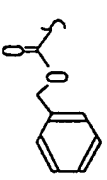
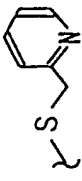
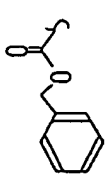
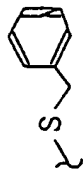
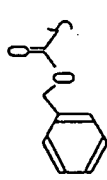
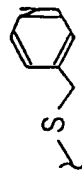
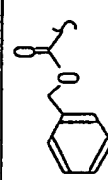
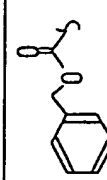
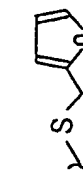
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16		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
17		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
18		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
19		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	-S-CH ₃
20		H	-CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	

Table 1 (n=0) (continued)

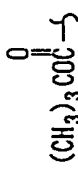
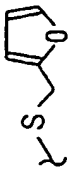
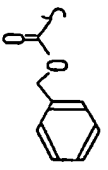
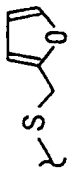
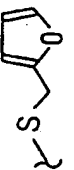
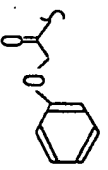
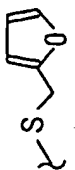
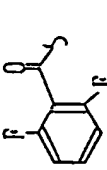
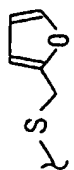
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
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2 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	
2 3	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	
2 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	
2 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	

Table 1 (n=0) (continued)

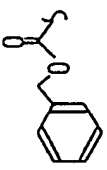
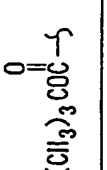
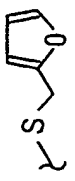
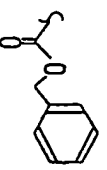
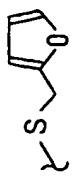
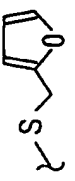
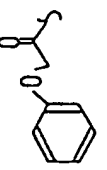
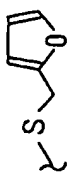
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
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2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
2 9	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	
3 3		H		H	-CH ₂ CH(CH ₃) ₂	H	
3 4		H	-CH ₃	H	-CH ₂ CH(CH ₃) ₂	H	
3 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 6		H		H	-CH ₂ CH(CH ₃) ₂	H	
3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
3 8		H	H	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
3 9		H	-CH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 0		H	-CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

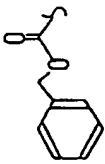
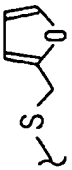
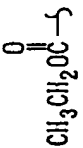
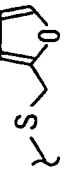
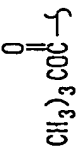
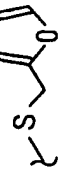
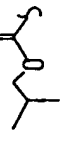
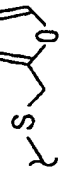
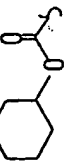
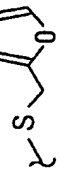
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 1		H	-CH ₂ CH ₂ Cl ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

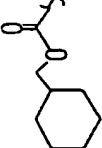
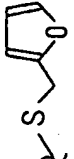

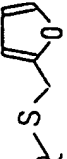
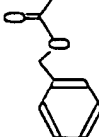
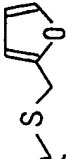
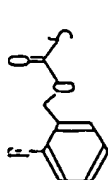
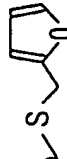
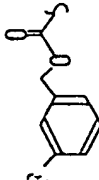
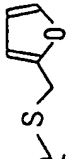
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
5 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

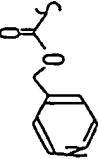
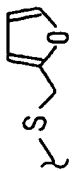
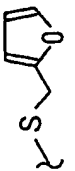

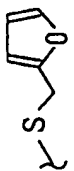
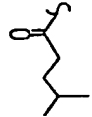
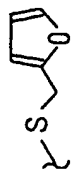
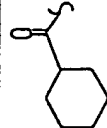
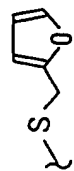
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 2	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

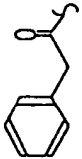
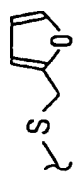
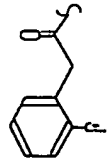
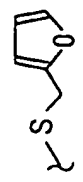
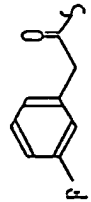
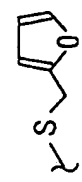
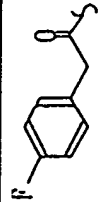
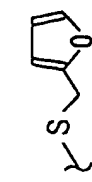
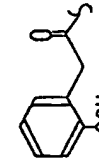
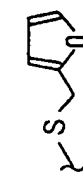
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
7 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7.3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

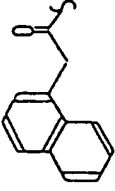
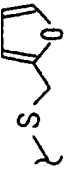
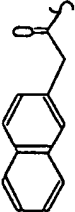
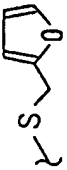

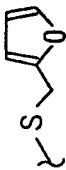

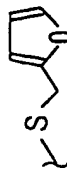

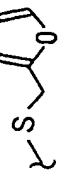
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
7 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

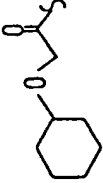
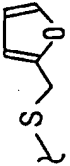
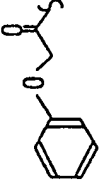
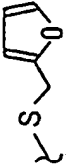
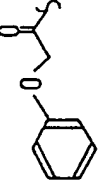
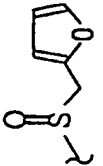
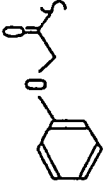
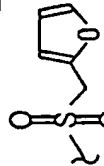
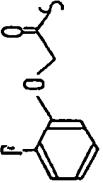
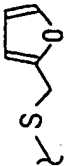
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
8 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

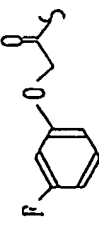
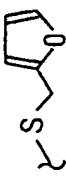
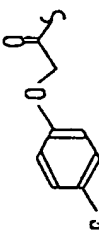
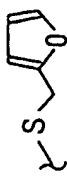
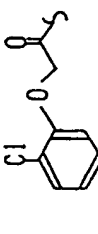
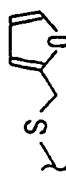
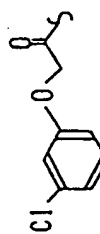
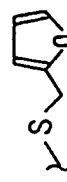
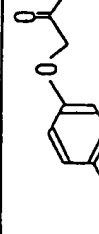
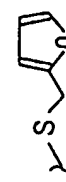
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
8 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
8 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
9 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

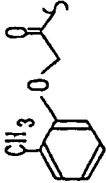
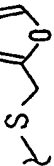
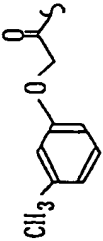

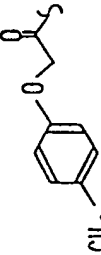
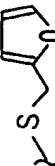
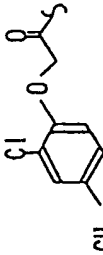

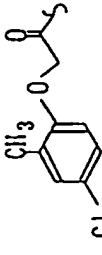

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
9 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
9 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 0 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

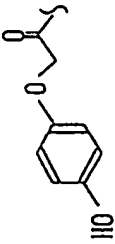
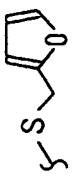
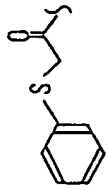
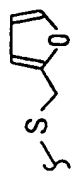

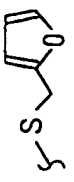
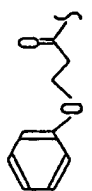
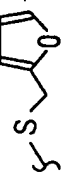
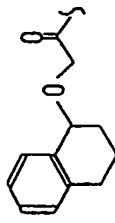
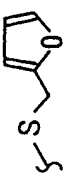
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 0 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 0 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 1 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

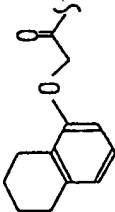
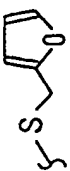
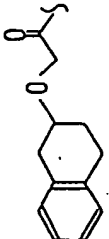
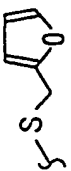
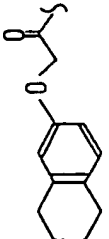
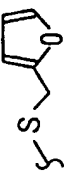
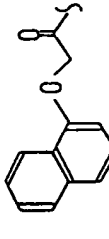
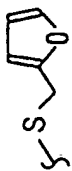
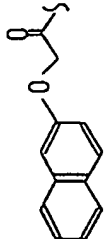
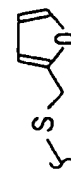
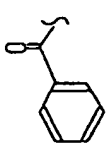
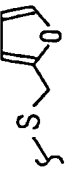
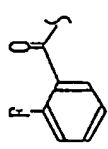
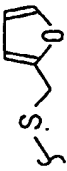
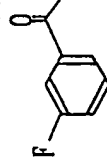
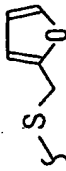
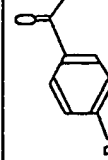
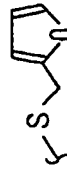
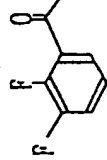
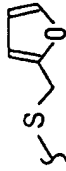
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 1 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 1 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 1 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 1 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 1 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
116		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
117		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
118		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
119		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
120		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

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Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

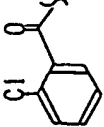
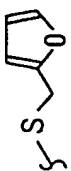
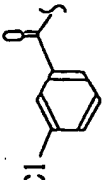
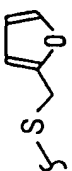
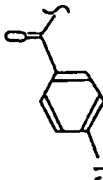
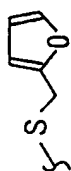
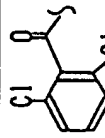
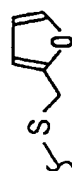
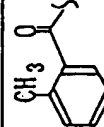
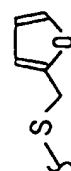
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 3 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 3 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

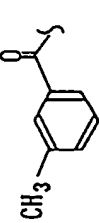
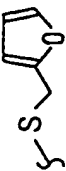
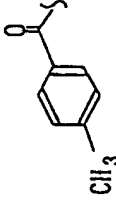
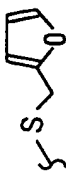
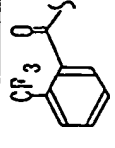
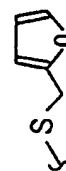
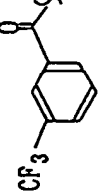
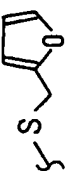
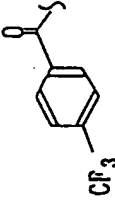
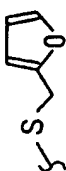
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 4 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 5 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 5 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 5 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 5 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 5 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
156		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
157		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
158		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
159		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
160		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

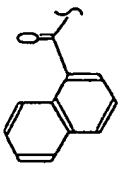
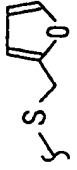
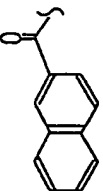
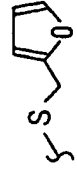
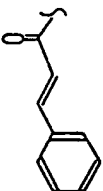
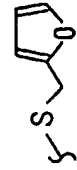
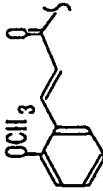
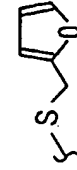
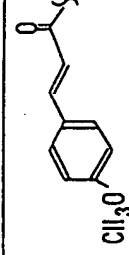
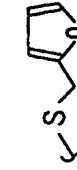
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 6 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 6 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 7 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

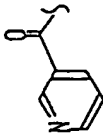
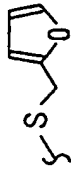
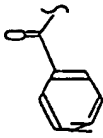
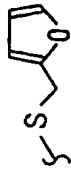
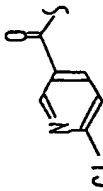
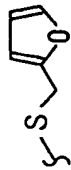
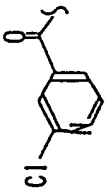
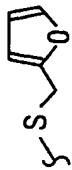
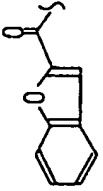
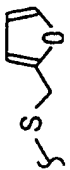
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 7 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 7 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 8 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

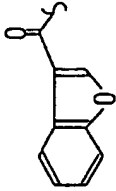
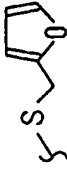
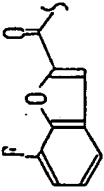
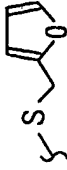

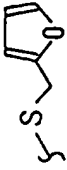

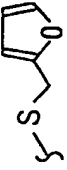
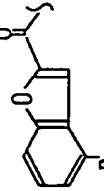
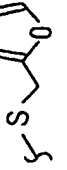
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
181		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
182		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
183		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
184		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
185		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

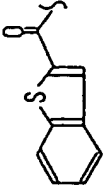
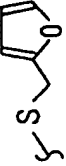
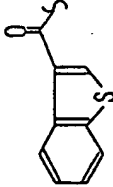
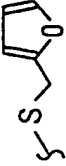
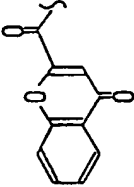
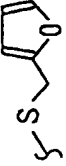
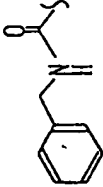
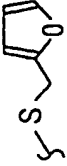
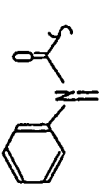
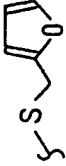
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 8 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 8 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1' 8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 8 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 9 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
191		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
192		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
193		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
194		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
195		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-O-CH ₃

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
1 9 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
1 9 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	S-N(CH ₃) ₂
1 9 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	S-N(CH ₂ CH ₃) ₂
1 9 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 0 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

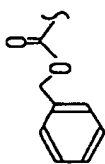

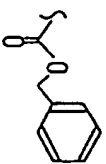

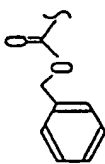

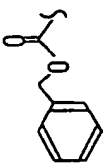

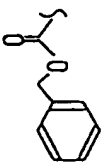
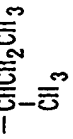
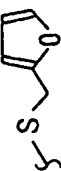
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 0 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 0 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 0 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 0 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 0 5		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

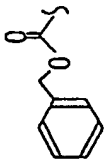
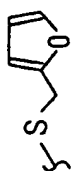
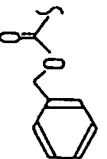


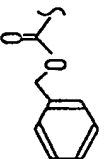
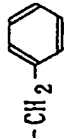
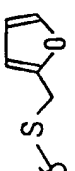
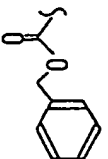
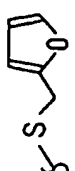
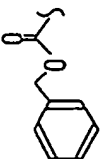
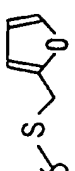
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
206		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
207		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
208		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
209		H	-CH ₂ OCH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
210		H	-CH ₂ OC(CH ₃) ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

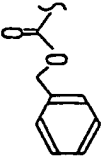
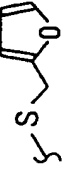
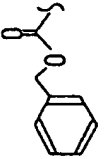
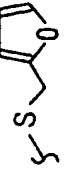
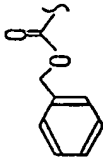
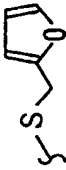
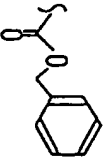
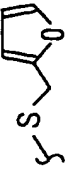
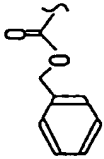
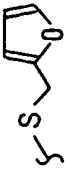
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 1 1		H	-CH ₂ OH	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 2		H	-CH ₂ COOCH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 3		H	-CH ₂ COOC(CH ₃) ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 4		H	-CH ₂ COOH	H	-CH ₂ CH ₂ CH ₂ CHCl ₃	H	
2 1 5		H	-CH ₂ CH ₂ COOCH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

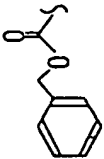
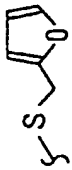
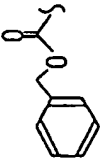
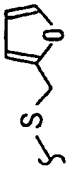
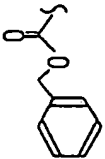

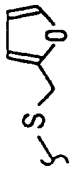
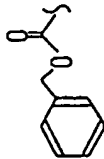

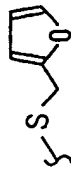
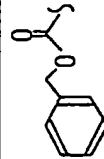
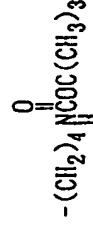
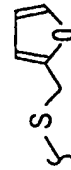
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 1 6		H	-CH ₂ CH ₂ COOC(CH ₃) ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 7		H	-CH ₂ CH ₂ COOH	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 8		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 1 9		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 2 0		H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

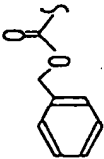
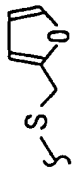
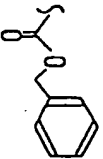
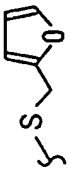
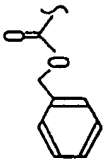
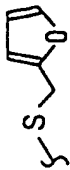
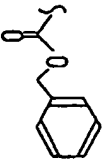

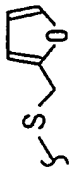
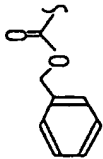
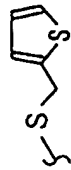
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 2 1		H	$-(CH_2)_4NH_2$	H	$-CH_2CH_2CH_2CH_3$	H	
2 2 2		H	$-(CH_2)_4NC(=O)CH_3$	H	$-CH_2CH_2CH_2CH_3$	H	
2 2 3		H	$-CH_2CH_2SCH_3$	H	$-CH_2CH_2CH_2CH_3$	H	
2 2 4		H		H	$-CH_2CH_2CH_2CH_3$	H	
2 2 5		H	$-CH_2CH(CH_3)_2$	H	$-CH_2CH_2CH_2CH_3$	H	

Table 1 (n=0) (continued)

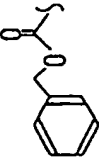
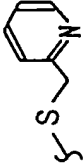
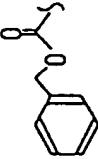
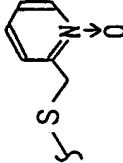
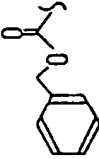
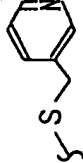
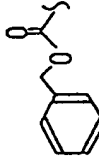
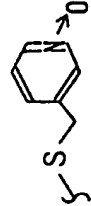
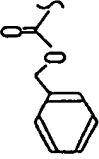
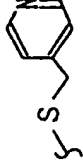
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

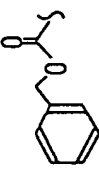
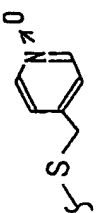
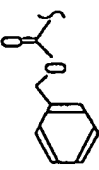
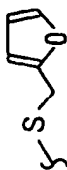
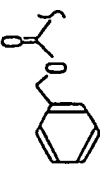
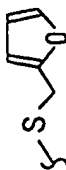
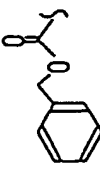
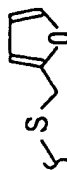
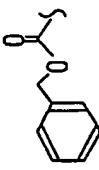

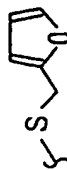
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 3 2		H	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 3 3		-CH ₃	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 3 4		-CH ₃	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ CH ₂ CH ₂ CH ₃	H	
2 3 5		H	-CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

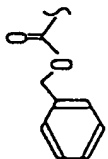

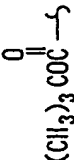

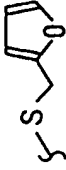
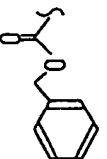

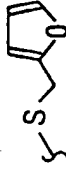

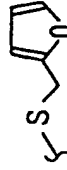
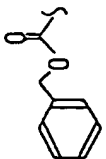

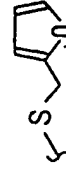
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 3 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 3 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 3 9	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 4 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

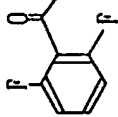

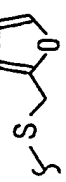
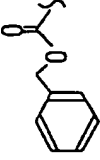

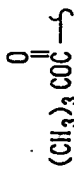

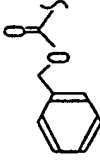

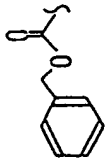

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 4 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 4 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-H
2 4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 4 5		H	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

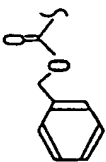

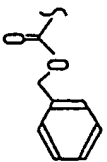

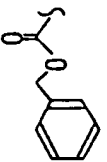

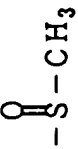
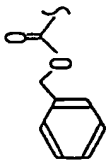

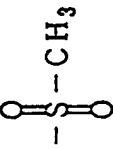

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 4 6		-CH ₃	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 4 7		-CH ₃	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ - 	H	-S-CH ₃
2 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 5 0	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

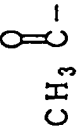

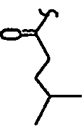

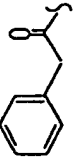

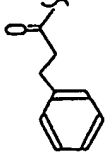

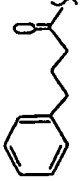

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 5 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

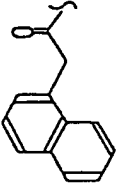

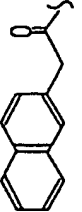

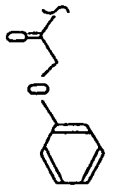

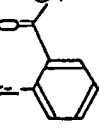

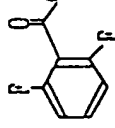

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 5 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 5 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 6 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

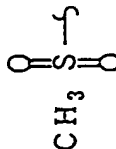

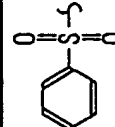

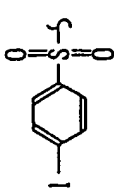

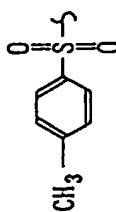

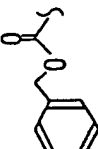

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 6 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
2 6 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₃

Table 1 (n=0) (continued)

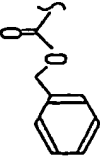
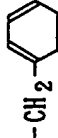
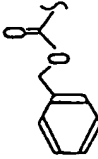
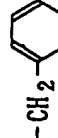
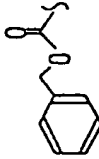
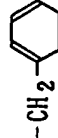
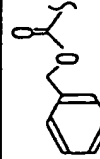
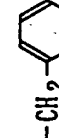
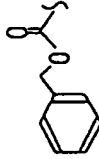
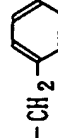
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 6 6		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-(CH ₂) ₃ CH ₃
2 6 7		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-(CH ₂) ₅ CH ₃
2 6 8		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-(CH ₂) ₇ CH ₃
2 6 9		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-(CH ₂) ₁₁ CH ₃
2 7 0		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-(CH ₂) ₁₃ CH ₃

Table 1 (n=0) (continued)

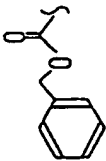

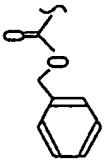

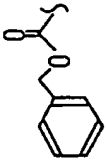

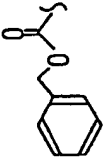

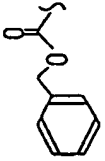

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
271		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ Cl
272		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ OCH ₃
273		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ OH
274		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ SCH ₃
275		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ N(CH ₃) ₂

Table 1 (n=0) (continued)

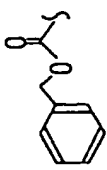


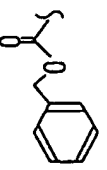


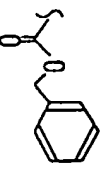


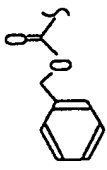


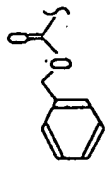

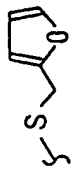
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
276		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ CH ₂ - 
277		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ - 
278		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₂ -CH ₂ - 
279		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S- 
280		H	H	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

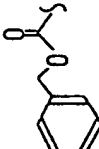


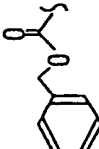

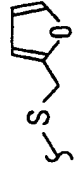
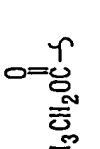

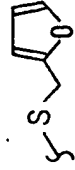
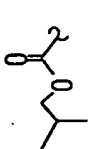

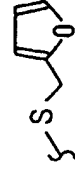
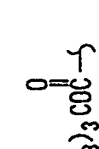

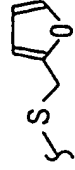
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 8 1		H	-CH ₃	H	-CH ₂ - 	H	
2 8 2		H	-CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)



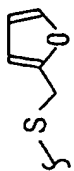


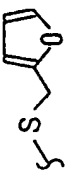
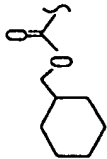

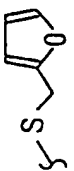
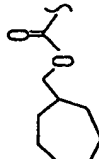

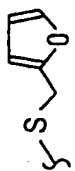


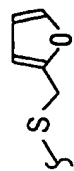
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 8 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 8 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 9 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 9 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
2 9 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
2 9 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
2 9 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
2 9 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 0 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

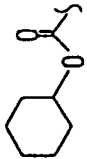

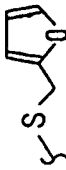
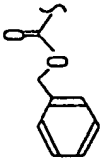

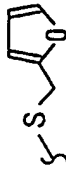
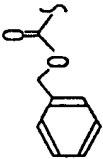

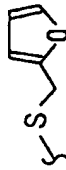
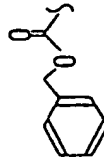

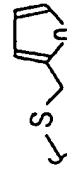
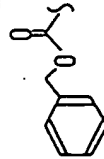

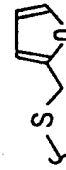
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
2 9 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 9 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
2 9 8		H	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ - 	H	
2 9 9		-CH ₃	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 0 0		-CH ₃	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 0 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 0 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 1 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

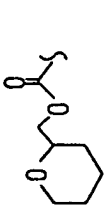


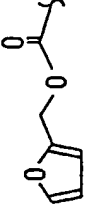

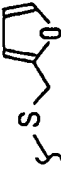
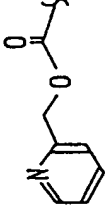


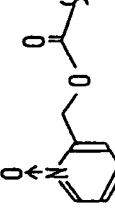


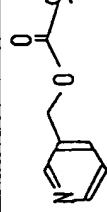

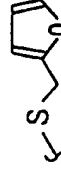
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 1 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

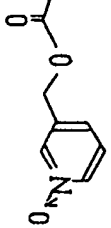

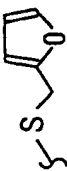
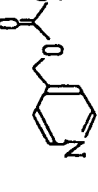

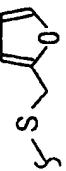
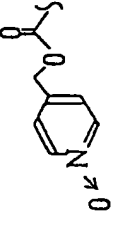

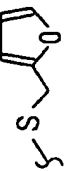


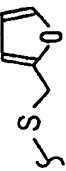
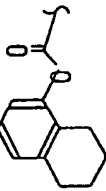

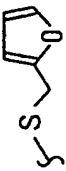
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 1 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 1 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

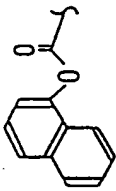

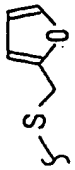
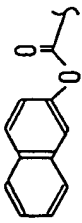

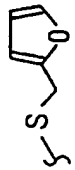

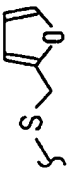
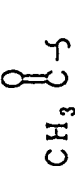

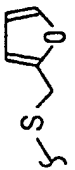
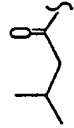

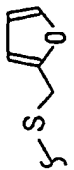
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 2 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 3	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

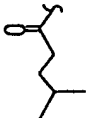

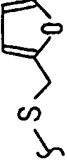
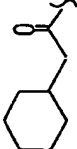

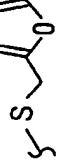
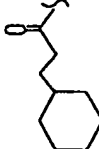

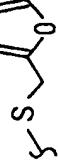
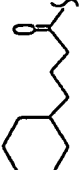

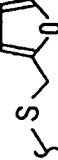
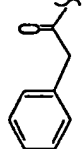

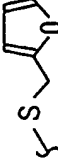
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 3 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 3 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 3 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

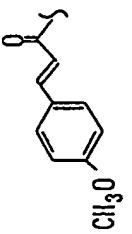

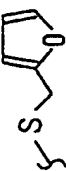
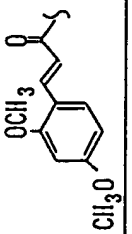

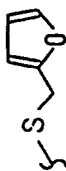
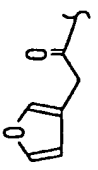

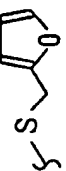


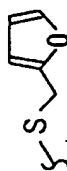
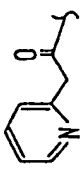

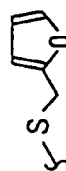
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 3 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 3 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 3 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)



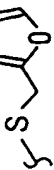
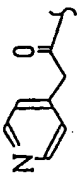

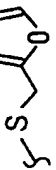


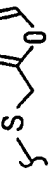
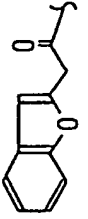

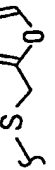


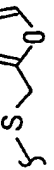
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 4 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)



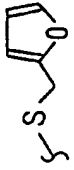
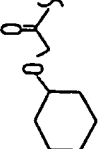

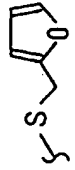
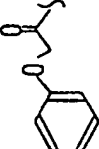

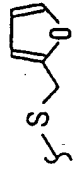
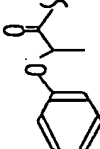

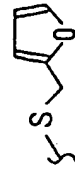
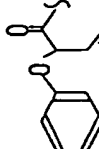

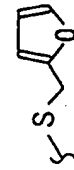
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 5 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 5 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 5 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 6 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -C ₆ H ₅	H	
3 6 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -C ₆ H ₅	H	
3 6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -C ₆ H ₅	H	
3 6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -C ₆ H ₅	H	
3 6 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -C ₆ H ₅	H	

Table 1 (n=0) (continued)

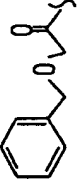
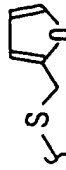
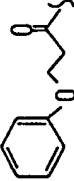
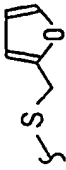
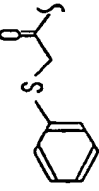
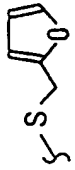
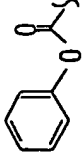
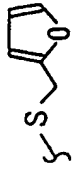
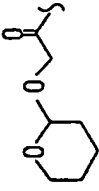
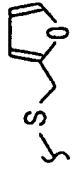
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 6 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 6 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 6 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 6 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 7 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

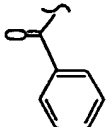

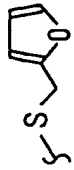
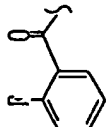

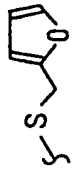
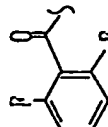

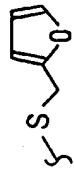
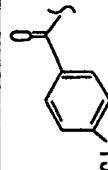

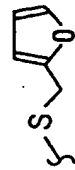
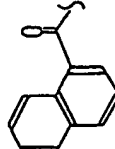

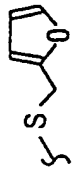
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 7 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

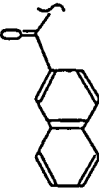

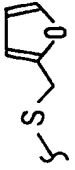
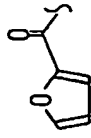

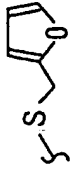
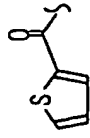

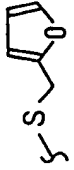
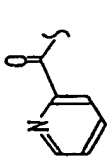

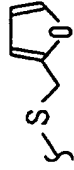
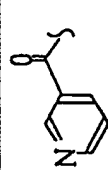

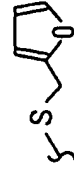
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 7 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 7 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

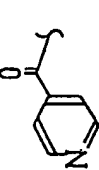

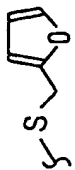
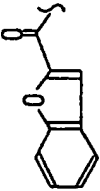

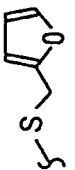
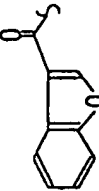

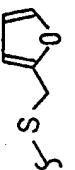
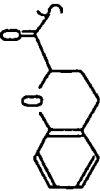

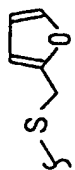
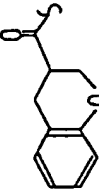

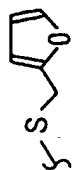
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 8 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

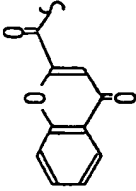

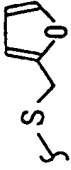
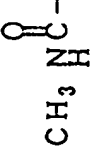

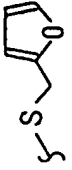
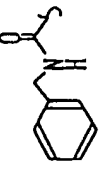

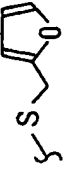
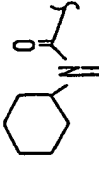

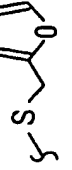
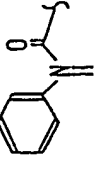

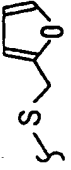
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 8 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 8 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
3 9 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

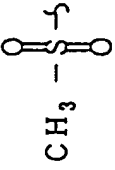

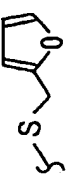
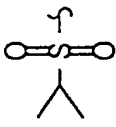
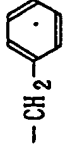
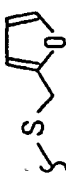
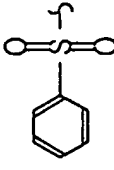
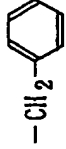
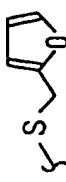
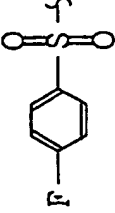
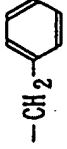
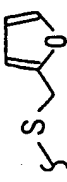
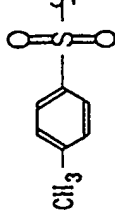
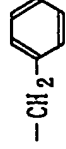
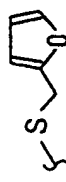
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 9 1		H	-CH ₂ CH(CH ₃) ₂	H		H	
3 9 2		H	-CH ₂ CH(CH ₃) ₂	H		H	
3 9 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
3 9 4		H	-CH ₂ CH(CH ₃) ₂	H		H	
3 9 5		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
3 9 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 9 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
3 9 8		H		H	-CH ₂ -	H	
3 9 9		H	-CH ₂ CH ₂ CH ₂ CHCl ₃	H	-CH ₂ -	H	
4 0 0		H		H	-CH ₂ -	H	

Table 1 (n=0) (continued)

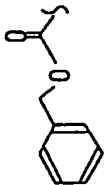
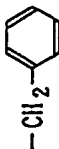
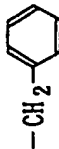
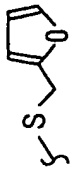
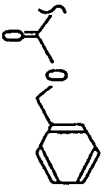
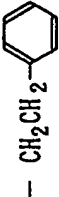

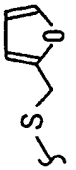
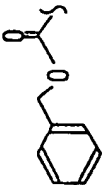

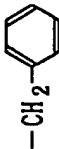
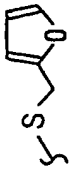
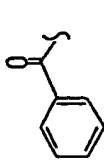

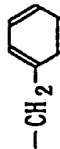
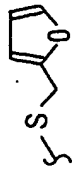
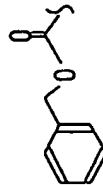

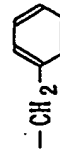
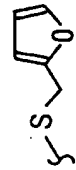
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 0 1		H		H		H	
4 0 2		H		H		H	
4 0 3		H		H		H	
4 0 4		H		H		H	
4 0 5		H		H		H	

Table 1 (n=0) (continued)

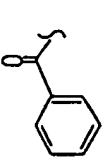

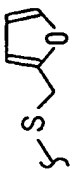
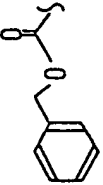

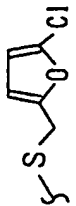
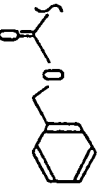


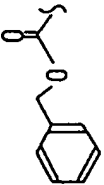

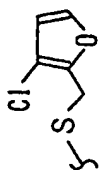
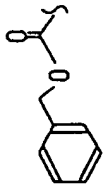

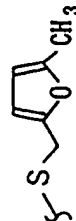
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 0 6		H	-OCH(CH ₃) ₂	H	-CH ₂ - 	H	
4 0 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 0 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 0 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

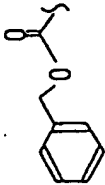

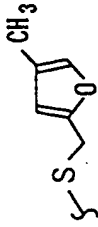
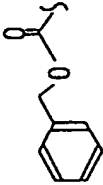

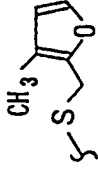
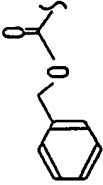

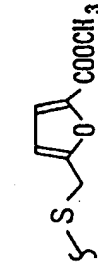
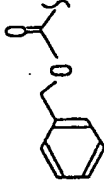

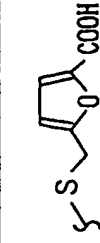
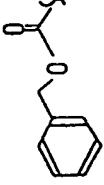

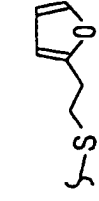
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 1 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

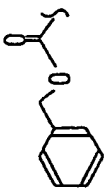

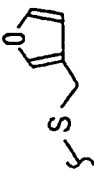
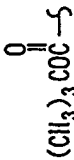

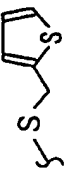
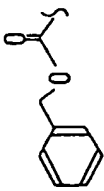

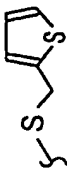

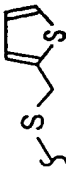
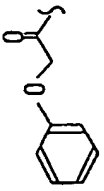

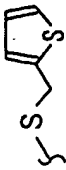
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 1 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 1 9	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 2 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 2 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 2 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 2 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 2 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 2 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

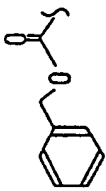

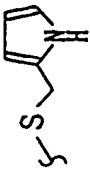
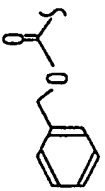

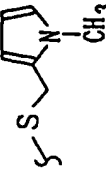
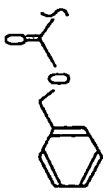

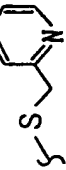
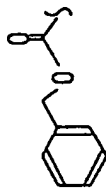

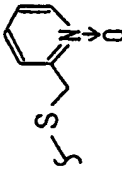
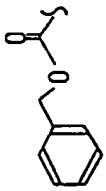

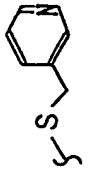
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

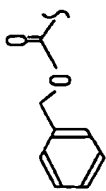

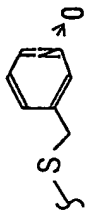
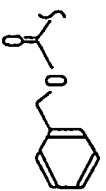

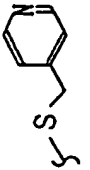
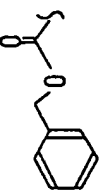

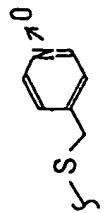
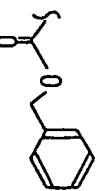

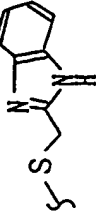
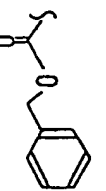

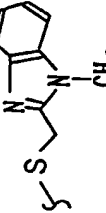
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

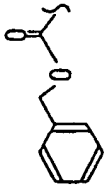

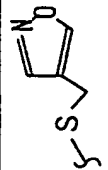
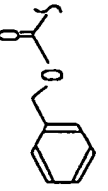

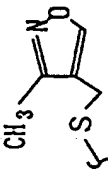
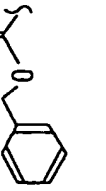

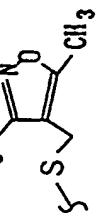


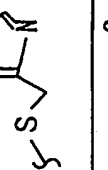


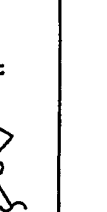
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 3 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 3 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 4 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

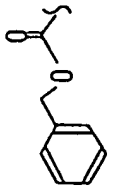
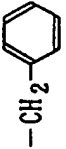
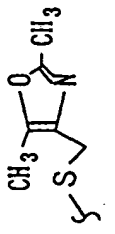
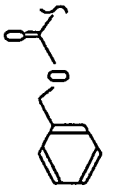
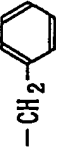

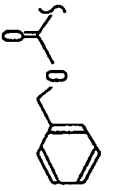
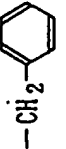
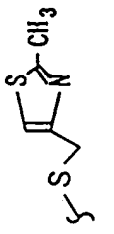
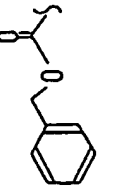
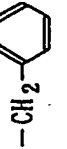


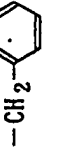
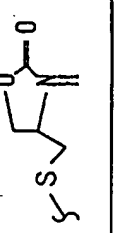
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 4 1		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 4 2		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 4 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 4 4		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 4 5		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

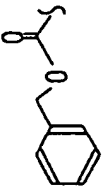

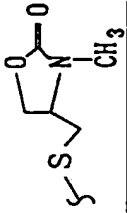
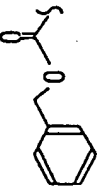

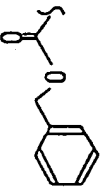

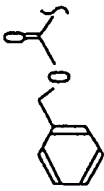

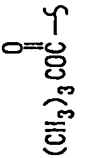

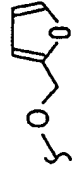
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-O-CH ₃
4 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-O-CH ₂ CH ₃
4 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-O-CH ₂ CH ₂ CH ₃
4 5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

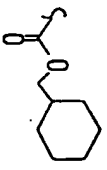

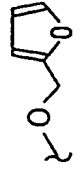
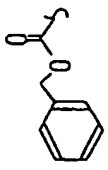

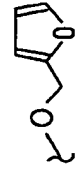
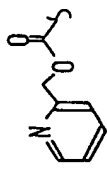

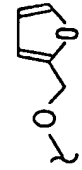

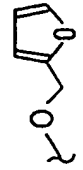
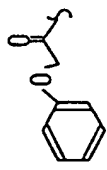

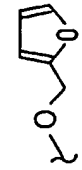
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 5 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 5 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 5 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 5 4	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 5 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 5 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 5 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 5 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 5 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
4 6 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

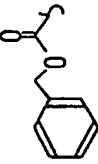

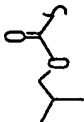

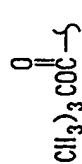

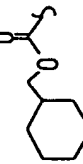

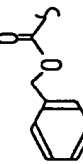

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-NH(CH ₃)
4 6 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 6 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 6 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-N(CH ₃) ₂
4 6 7	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-N(CH ₃) ₂
4 6 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-N(CH ₃) ₂
4 6 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-N(CH ₃) ₂
4 7 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-N(CH ₃) ₂

Table 1 (n=0) (continued)

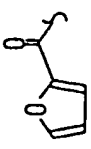

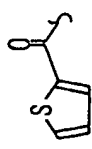

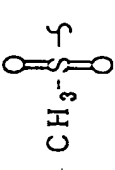

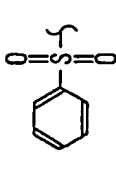

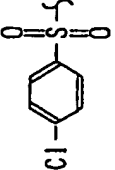

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 7 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 7 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 7 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 7 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂
4 7 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-N(CH ₃) ₂

Table 1 (n=0) (continued)

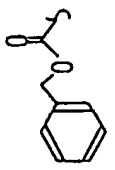

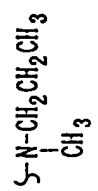
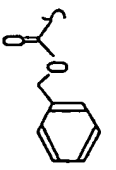

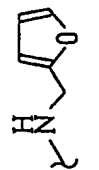
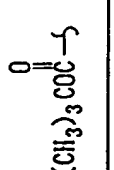

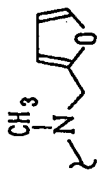
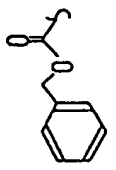

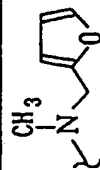

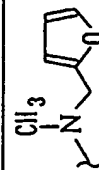
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 7 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 7 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 7 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 7 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 0	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

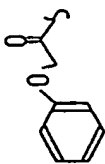

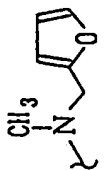
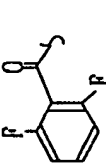

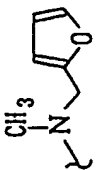
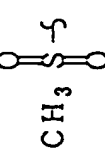

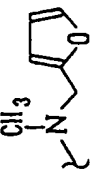
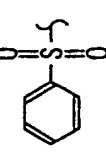

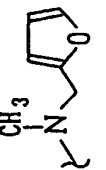
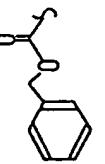

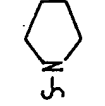
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 8 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

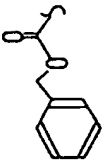


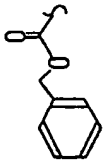

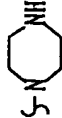
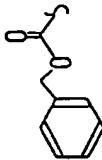

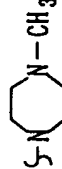
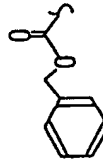

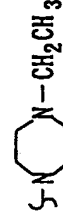
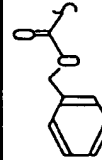

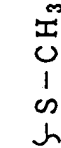
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 8 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 8 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
4 9 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
4 9 1		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 9 2		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
4 9 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
4 9 4		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
4 9 5		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
496		H	-CH ₂ CH(CH ₃) ₂	H		H	
497	H	H	-CH ₂ CH(CH ₃) ₂	H		H	
498		H	-CH ₂ CH(CH ₃) ₂	H		H	
499		H	-CH ₂ CH(CH ₃) ₂	H		H	
500		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

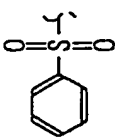
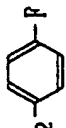
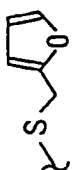
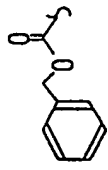
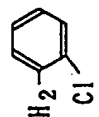
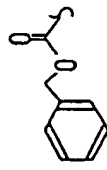
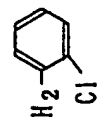
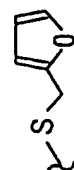
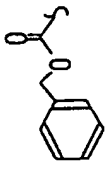
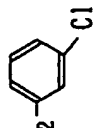
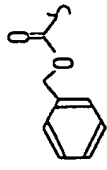
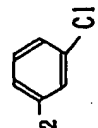
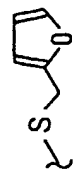
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
501		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
502		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
503		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
504		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
505		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

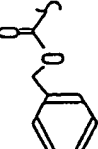
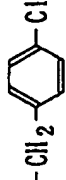
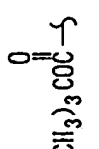
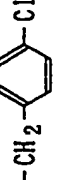
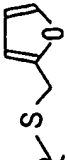
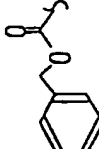
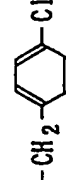
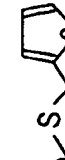
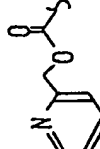
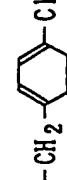
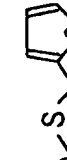
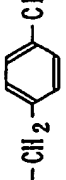
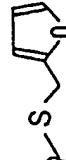
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
506		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
507		H	-CH ₂ CH(CH ₃) ₂	H		H	
508		H	-CH ₂ CH(CH ₃) ₂	H		H	
509		H	-CH ₂ CH(CH ₃) ₂	H		H	
510	H	H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)


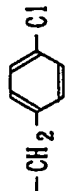
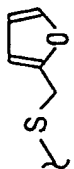
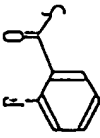
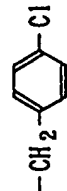
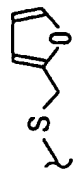
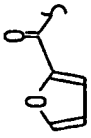
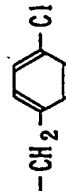
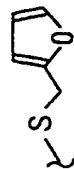
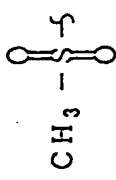
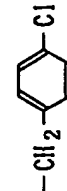
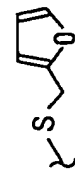
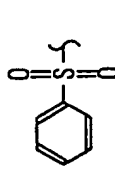
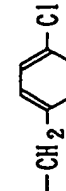
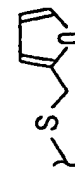
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
511		H	-CH ₂ CH(CH ₃) ₂	H		H	
512		H	-CH ₂ CH(CH ₃) ₂	H		H	
513		H	-CH ₂ CH(CH ₃) ₂	H		H	
514		H	-CH ₂ CH(CH ₃) ₂	H		H	
515		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

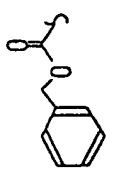
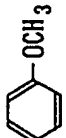
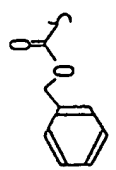
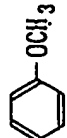
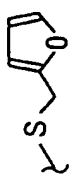
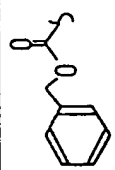
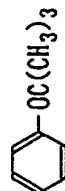
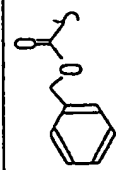
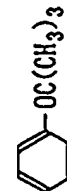
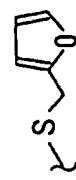
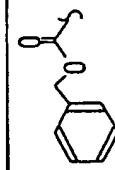
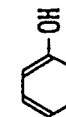
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
516		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
517		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
518		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
519		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
520		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

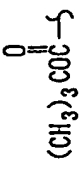
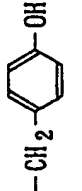
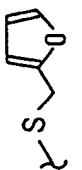
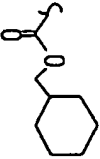
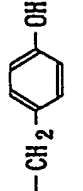
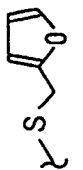
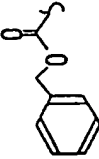
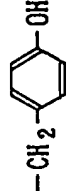
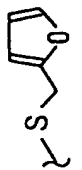
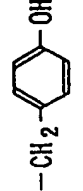
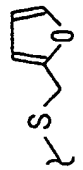

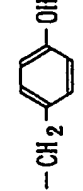
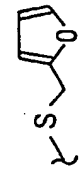
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 2 1		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 2 2		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 2 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 2 4	H	H	-CH ₂ CH(CH ₃) ₂	H		H	
5 2 5		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

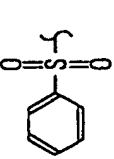
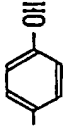
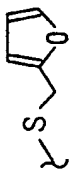
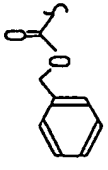

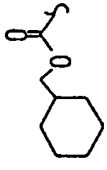

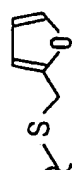
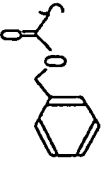

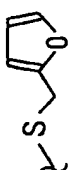
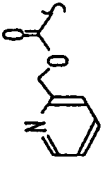

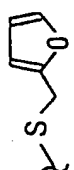
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
5 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
5 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
5 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
5 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

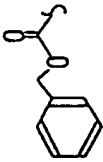
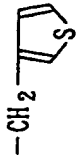
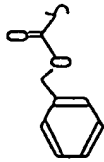
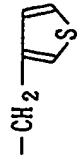
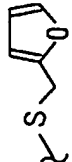
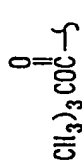

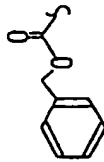
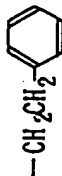
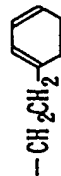
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 3 1		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 3 2		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 3 3		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 3 4		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 3 5	H	H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
536		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	-S-CH ₃
537		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	-S-CH ₃
538		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
539		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
540		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 4 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
5 4 2	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
5 4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
5 4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	
5 4 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -	H	

Table 1 (n=0) (continued)

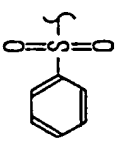

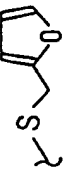
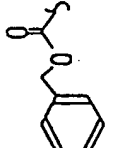
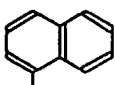
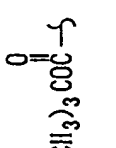
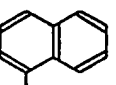
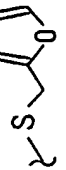
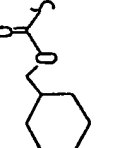
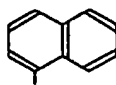
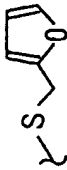
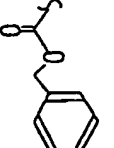
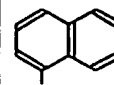
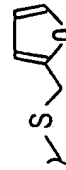
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	
5 4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
5 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
5 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
5 5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 5 1		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 5 2		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 5 3	H	H	-CH ₂ CH(CH ₃) ₂	H		H	
5 5 4		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 5 5		H	-CH ₂ CH(CH ₃) ₂	H		H	

Table 1 (n=0) (continued)

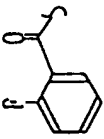
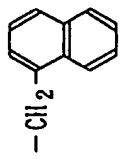
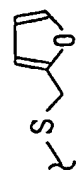
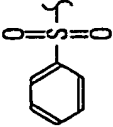
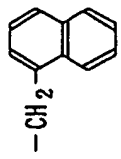
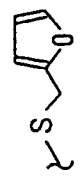
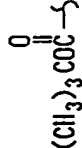
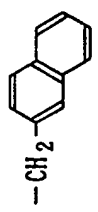
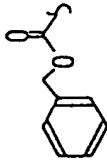
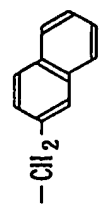
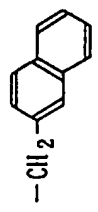
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 5 6		H	-CH ₂ CH(ClCH ₃) ₂	H		H	
5 5 7		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 5 8		H	-CH ₂ CH(ClCH ₃) ₂	H		H	-S-CH ₃
5 5 9		H	-CH ₂ CH(ClCH ₃) ₂	H		H	-S-CH ₃
5 6 0	H	H	-CH ₂ CH(ClCH ₃) ₂	H		H	-S-CH ₃

Table 1 (n=0) (continued)

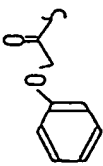
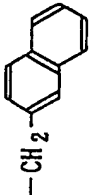
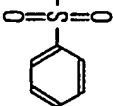
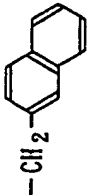
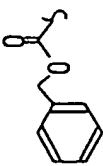
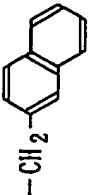
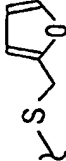
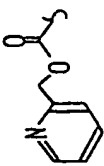
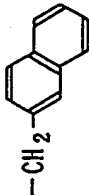
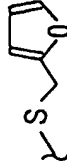
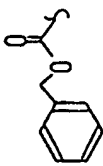

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 6 1		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 6 2		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 6 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 6 4		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 6 5		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃

Table 1 (n=0) (continued)

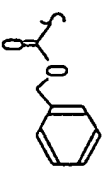

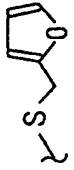
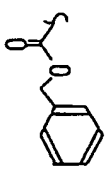
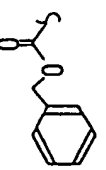
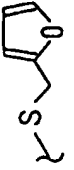
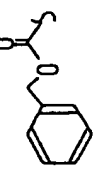
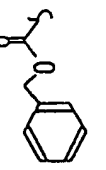
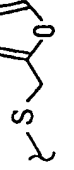
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 6 6		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 6 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	-S-CH ₃
5 6 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
5 6 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	-S-CH ₃
5 7 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

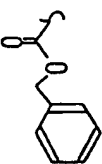

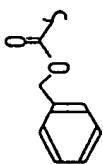

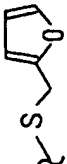
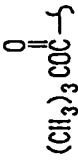

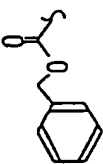


Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 7 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	-S-CH ₃
5 7 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	
5 7 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	-S-CH ₃
5 7 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	-S-CH ₃
5 7 5	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)



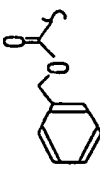

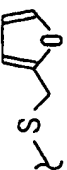
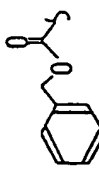
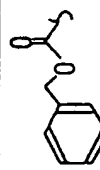
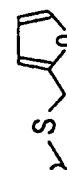
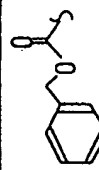
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
576		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	-S-CH ₃
577		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	
578		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	-S-CH ₃
579		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	
580		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₃	H	-S-CH ₃

Table 1 (n=0) (continued)

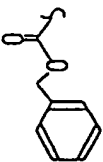
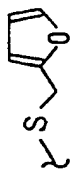
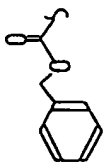
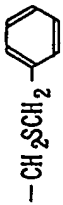
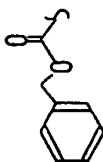
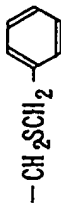
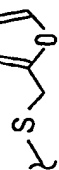
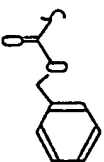
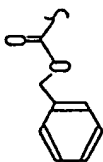
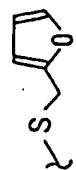
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 8 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ SCH ₂ CH ₃	H	
5 8 2		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 8 3		H	-CH ₂ CH(CH ₃) ₂	H		H	
5 8 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ SCH ₂ SCH ₃	H	-S-CH ₃
5 8 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ SCH ₂ SCH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
5 8 6		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 8 7		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 8 8		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 8 9	H	H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
5 9 0		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃

Table 1 (n=0) (continued)

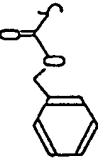
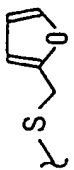
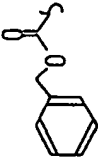
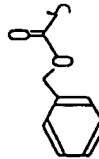
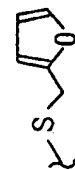
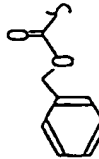
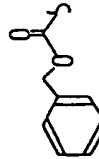
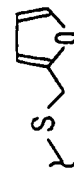
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
596		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ COOH	H	
597		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ COOCH ₃	H	-S-CH ₃
598		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ COOCH ₃	H	
599		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ COOH	H	-S-CH ₃
600		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ COOH	H	

Table 1 (n=0) (continued)

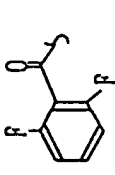

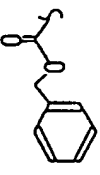

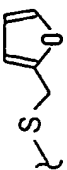
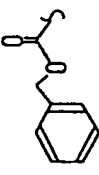
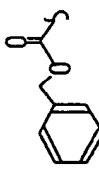
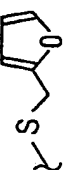
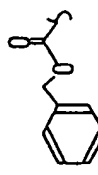
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
591		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ S- CH ₂ - 	H	-S-CH ₃
592		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ S- CH ₂ - 	H	
593		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ COOCH ₃	H	-S-CH ₃
594		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ COOCH ₃	H	
595		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ COOH	H	-S-CH ₃

Table 1 (n=0) (continued)

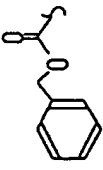
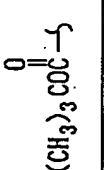
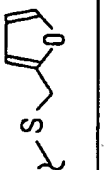
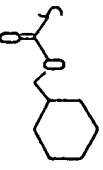
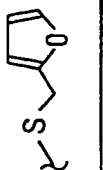
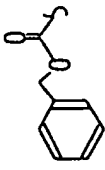
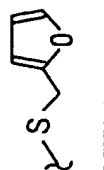
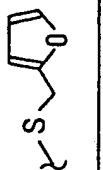
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 0 1		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 0 2		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	
6 0 3		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	
6 0 4		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	
6 0 5	H	H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
606		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ CH ₂ CH ₃	H	
607		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ -		-S-CH ₃
608		H	-CH ₂ CH(CH ₃) ₂	H	-OCH ₂ -		
609		H	-CH ₂ CH(CH ₃) ₂	H			-S-CH ₃
610		H	-CH ₂ CH(CH ₃) ₂	H			

Table 1 (n=0) (continued)

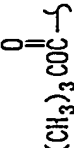
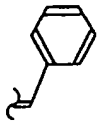
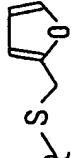
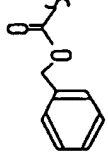
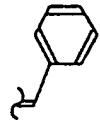
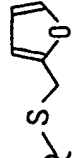
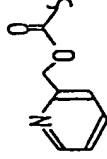
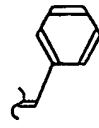
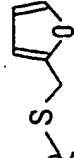
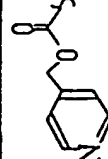
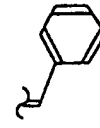
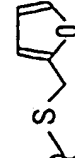
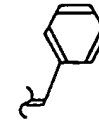
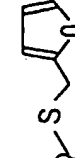
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 1 1		H	-CH ₂ CH(CH ₃) ₂	H			
6 1 2		H	-CH ₂ CH(CH ₃) ₂	H			
6 1 3		H	-CH ₂ CH(CH ₃) ₂	H			
6 1 4		H	-CH ₂ CH(CH ₃) ₂	H			
6 1 5	H	H	-CH ₂ CH(CH ₃) ₂	H			

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
616		H	-CH ₂ CH(CH ₃) ₂	H			
617		H	-CH ₂ CH(CH ₃) ₂	H			
618		H	-CH ₂ CH(CH ₃) ₂	H			
619		H	-CH ₂ CH(CH ₃) ₂	H			
620		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -		-S-CH ₃

Table 1 (n=0) (continued)

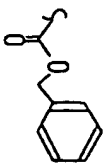
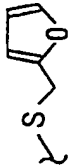
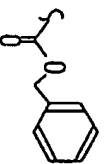
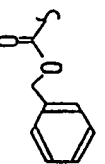
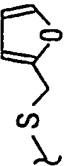
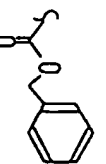
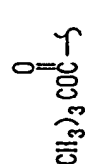
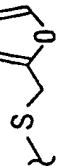
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 2 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ -		
6 2 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ -		-S-CH ₃
6 2 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ -		
6 2 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		-S-CH ₃
6 2 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		

Table 1 (n=0) (continued)

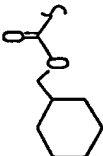
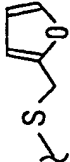
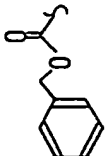
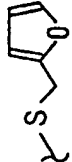
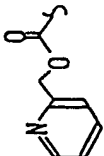
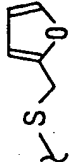
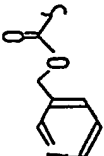
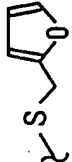
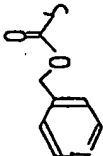
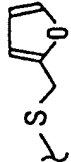
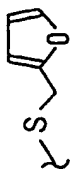
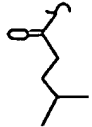
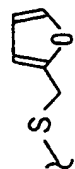
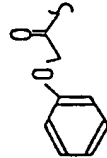
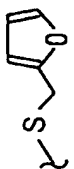
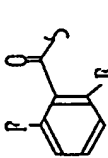
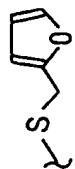
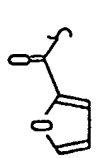
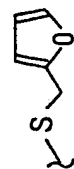
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 3 1	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 3 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 3 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 4 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		

Table 1 (n=0) (continued) :

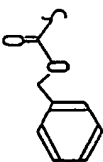
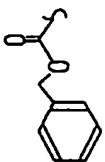
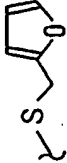
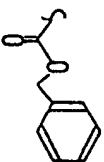

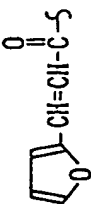
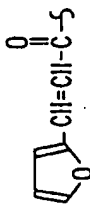
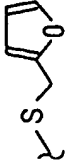
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 4 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		-O-CH ₃
6 4 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 4 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -		
6 4 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -	H	-S-CH ₃
6 4 5		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ -	H	

Table 1 (n=0) (continued)

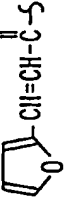



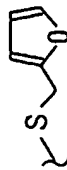
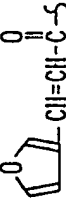
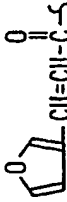
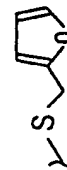
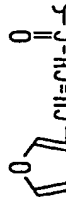

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 4 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃
6 4 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
6 4 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 4 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 5 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹	
6 5 1			H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	
6 5 2			H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 5 3			H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 5 4			H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-S-CH ₃
6 5 5			H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 5 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 5 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 5 8		H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃
6 5 9		H	-CH ₂ CH(CH ₃) ₂	H		H	
6 6 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)


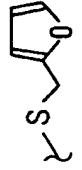

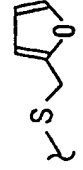

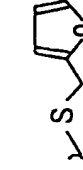

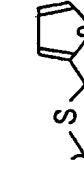

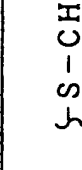
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 6 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 6 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 6 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 6 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 6 5		-CH ₂ CH ₂ CH ₂ -		H	-CH ₃	H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 6 6		-CH ₂ CH ₂ CH ₂ -	-	H	-CH ₃	H	
6 6 7		-CH ₂ CH ₂ CH ₂ -	-	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 6 8		-CH ₂ CH ₂ CH ₂ -	-	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 6 9		-CH ₂ CH ₂ CH ₂ -	-	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 7 0	H	-CH ₂ CH ₂ CH ₂ -	-	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 1 (n=0) (continued)

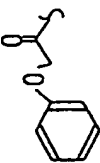
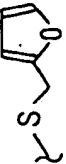
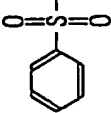
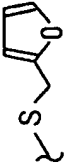
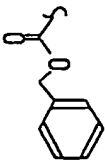

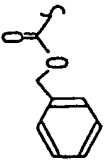

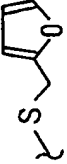
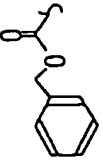
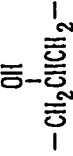

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 7 1			-CH ₂ CH ₂ CH ₂ -	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 7 2			-CH ₂ CH ₂ CH ₂ -	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 7 3			-CH ₂ CH ₂ CH ₂ -	H	-CH ₂ - 	H	-S-CH ₃
6 7 4			-CH ₂ CH ₂ CH ₂ -	H	-CH ₂ - 	H	
6 7 5			 -CH ₂ CH ₂ CH ₂ -	H	-CH ₂ - 	H	-S-CH ₃

Table 1 (n=0) (continued)

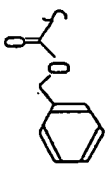
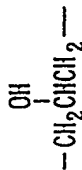
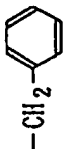
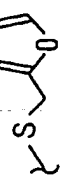
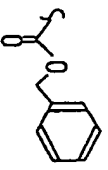
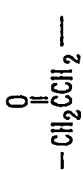
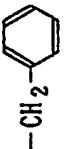
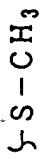
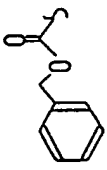
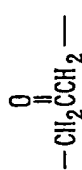
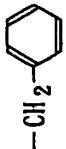
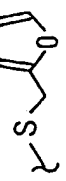
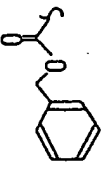

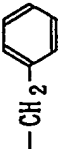
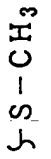
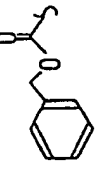

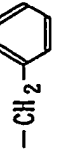
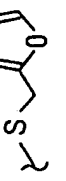
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 7 6				H		H	
6 7 7				H		H	
6 7 8				H		H	
6 7 9				H		H	
6 8 0				H		H	

Table 1 (n=0) (continued)

Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 8 1				H		H	
6 8 2				H		H	
6 8 3				H		H	
6 8 4	H			H		H	
6 8 5				H		H	

Table 1 (n=0) (continued)

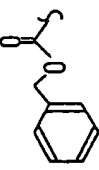
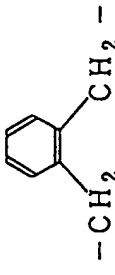
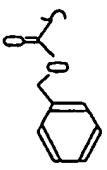
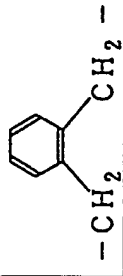
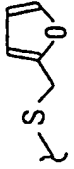
Compd. No.	R ¹	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 8 6				H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃
6 8 7				H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 2 (n=1)

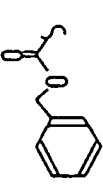
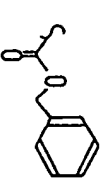
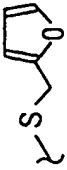
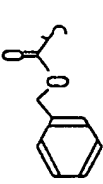
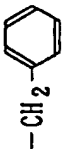
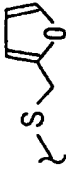
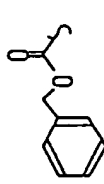
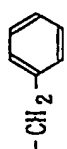
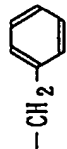
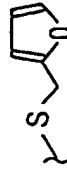
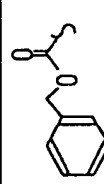
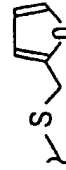
Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 8 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	H	-S-CH ₃
6 8 9		H	-CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	H	
6 9 0		H	-CH ₂ CH(CH ₃) ₂	H		H	-CH ₃	H	
6 9 1		H		H		H	-CH ₃	H	
6 9 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 2 (n=1) (continued)

Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 9 3		H	-CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9 4		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9 5		H	-CH ₃	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9 6		H	-CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	-S-CH ₃

Table 2 (n=1) (continued)

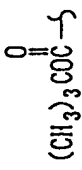
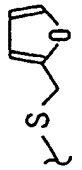
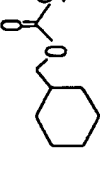
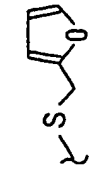
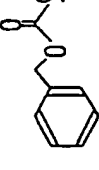
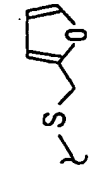
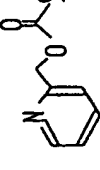
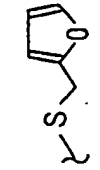
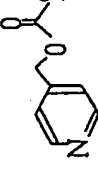
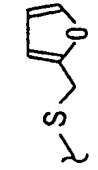
Compd, No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
6 9 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
6 9 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 0 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 0 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
7 0 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 2 (n=1) (continued)

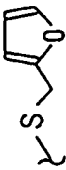
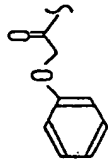
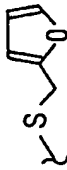
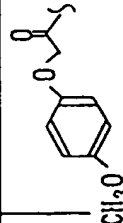
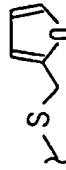
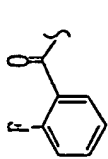
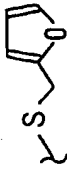
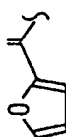
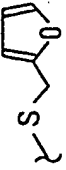
Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
703	H	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
704		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
705		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
706		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
707		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	

Table 2 (n=1) (continued)

Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
713		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
714		H	-CH ₂ CH(CH ₃) ₂	H		H	-CH ₂ CH ₂ CH ₂ CH ₃	H	
715		H	-CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H		H	
716		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H		H	
717		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H		H	-S-CH ₃

Table 2 (n=1) (continued)

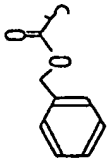


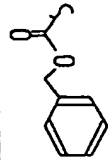

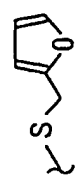
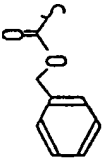

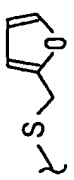
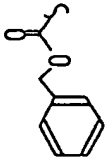

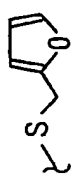
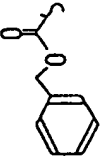

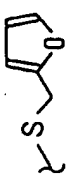
Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
718		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-CH ₂ - 	H	-S-CH ₃
719		H	-CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	-CH ₂ - 	H	
720		H	-CH ₂ CH(CH ₃) ₂	H	-CH(CH ₃) ₂	H	-CH ₂ - 	H	
721		H	-CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
722		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	

Table 2 (n=1) (continued)

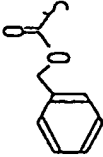

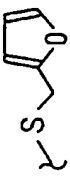
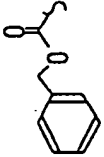

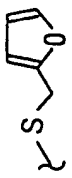
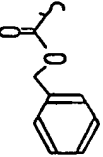

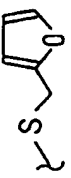
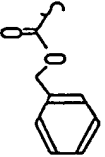


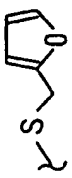
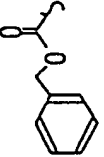

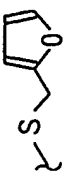
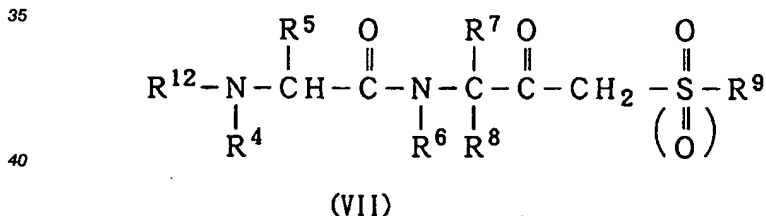
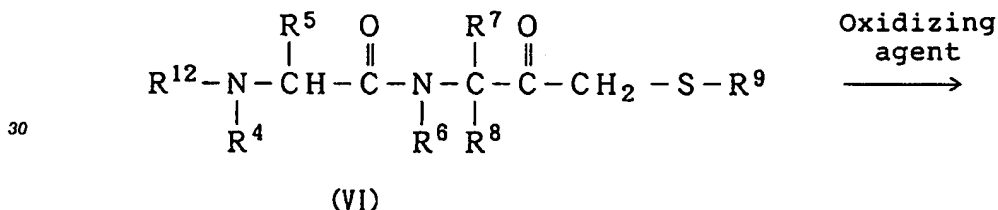
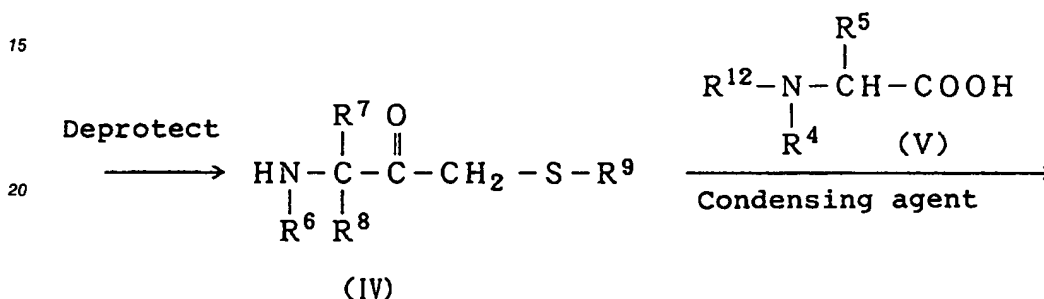
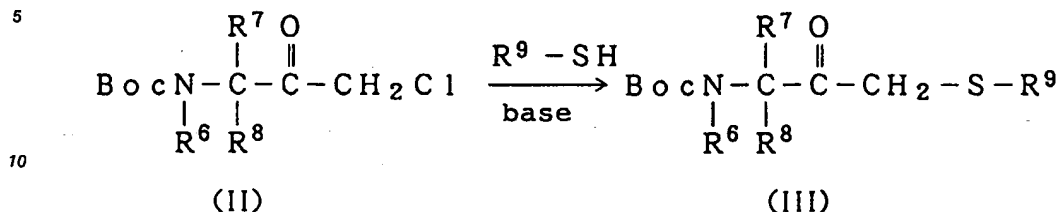
Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
7 2 3		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ - 	H	
7 2 4		H	-CH ₂ CH(CH ₃) ₂	-CH ₃	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
7 2 5		-CH ₃	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	
7 2 6		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ - 	H	-CH ₂ - 	H	
7 2 7		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH ₂ - 	H	

Table 2 (n=1) (continued)

Compd. No.	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸	-A-R ⁹
7 2 8		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ -	H	-CH ₃	-CH ₃	-S-CH ₃
7 2 9		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
7 3 0		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
7 3 1		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	
7 3 2		H	-CH ₂ CH(CH ₃) ₂	H	-CH ₂ CH(CH ₃) ₂	H	-CH ₃	-CH ₃	

The production of the compounds according to the present invention will be then explained. The ketone derivatives of the general formula (I) above can be, for example, prepared as shown below.

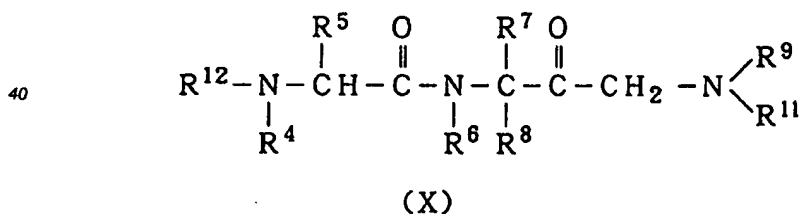
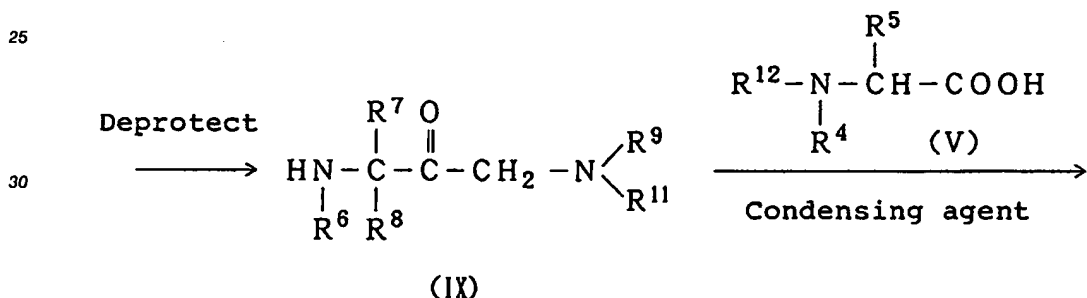
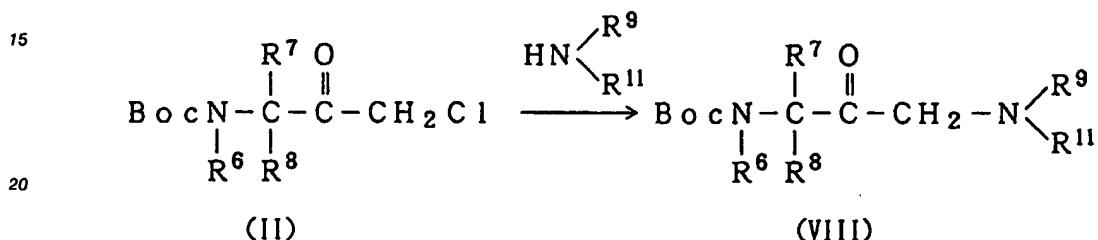
Preparation 1

[wherein R^4 , R^5 , R^6 , R^7 , R^8 and R^9 are as defined above, R^{12} is $\text{R}^{10}\text{-CO-}$, $\text{R}^{10}\text{-O-CO-}$, $\text{R}^{10}\text{-NH-CO-}$ or $\text{R}^{10}\text{-SO}_2\text{-}$ (R^{10} is as defined above), and Boc is tert-butoxycarbonyl group].

A chloromethylketone derivative of the general formula (II) above, which can be easily prepared using a known method in a literature [Chemical and Pharmaceutical Bulletin, 37, p.3108 (1989)], is dissolved in a solvent such as diethyl ether, tetrahydrofuran, dioxane, ethyl acetate, methylene chloride or chloroform, and reacted with a mercaptan of $\text{R}^9\text{-SH}$ in the presence of a base such as sodium hydroxide, potassium hydroxide, sodium hydride, triethylamine or pyridine to obtain a thiomethylketone derivative of the general formula (III). Boc group of the compound (III) is then deprotected by a conventional reaction condition, for example, using aqueous hydrochloric acid, hydrogen chloride-ethanol, hydrogen chloride-ethyl acetate,

hydrogen chloride-dioxane, hydrobromic acid, or hydrogen bromide-ethyl acetate, to obtain an amine or amine salt of the general formula (IV). Then, carboxyl group of an amino acid derivative of the general formula (V) is activated with a condensing agent such as isobutyl chloroformate, diphenylphosphorylazide, dicyclohexylcarbodiimide, or carbonyldiimidazole, and the activated amino acid derivative is reacted with the compound (IV) above obtained, if necessary, in the presence of a base such as triethylamine or pyridine, to obtain the compound of the general formula (VI). The compound (VI) is subsequently dissolved in a solvent such as chloroform, methylene chloride, methanol, ethanol, or ethyl acetate, dimethylformamide, dichloromethane, and oxidized its sulfide group to sulfoxide or sulfone group using sodium metaperiodate, hydrogen peroxide, peracetic acid, metachloroperbenzoic acid or the like to obtain the compound of the general formula (VII).

Preparation 2



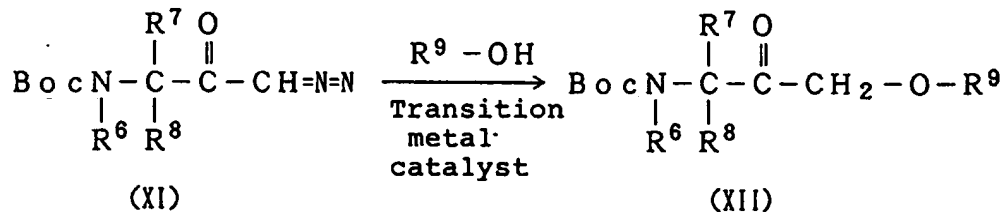
[wherein Boc, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹¹ and R¹² are as defined above]

A chloromethylketone derivative of the general formula (II) above is dissolved in a solvent such as diethyl ether, tetrahydrofuran, dioxane, ethyl acetate, chloroform or methylene chloride, and reacted with an amine of HN(R⁹)(R¹¹) to obtain a diaminoketone derivative of the general formula (VIII). In a similar procedure as described in Preparation 1, Boc group of the compound (VIII) is then deprotected to the compound of the general formula (IX), and the latter compound is condensed with the amino acid derivative of the general formula (V) to obtain the compound of the general formula (X).

Preparation 3

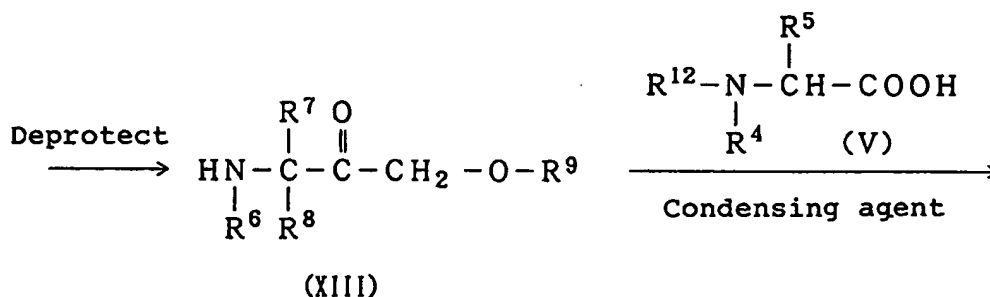
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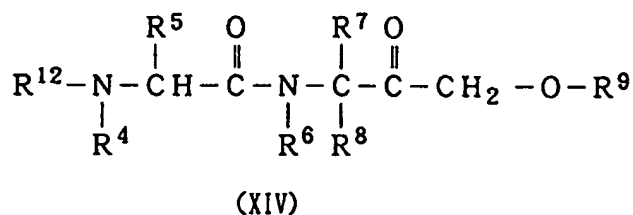
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[wherein Boc, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹ and R¹² are as defined above]

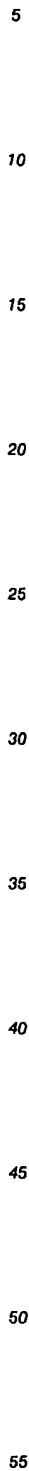
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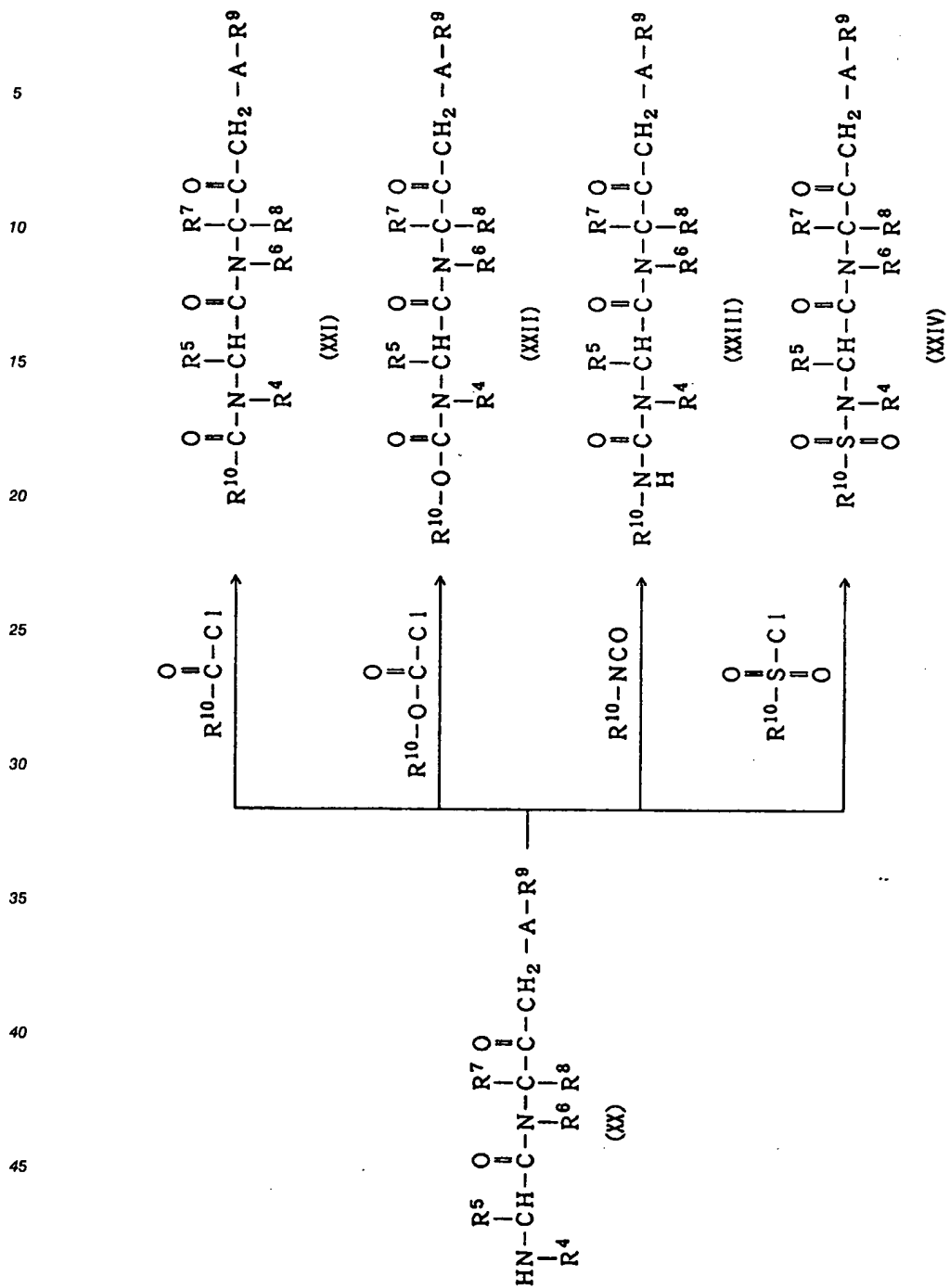
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A diazomethylketone derivative of the general formula (XI) above, which can be easily prepared using a known method in a literature [Methods in Enzymology, 80, p.820 (1981)], is dissolved in a solvent such as chloroform or methylene chloride, and reacted with an alcohol of R⁹-OH in the presence of a transition metal catalyst such as CuO or Rh₂(OAc)₄ to obtain a oxymethylketone derivative of the general formula (XII). In this case, it is also possible to carry out the reaction by directly dissolving the compound of the formula (XI) in alcohol: R⁹-OH without using the solvent such as chloroform or methylene chloride. Subsequently, in a similar procedure as described in Preparation 1, Boc group of the compound (XII) is deprotected to the compound (XIII), and the latter compound is condensed with the amino acid derivative of the general formula (V) to obtain the compound of the general formula (XIV).

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[wherein Boc, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹ and A are as defined above]

In a similar procedure as described in Preparation 1, Boc group of the compounds of the general formulae (XVI) to (XIX), which can be prepared using the compound of the formula (XV) instead of that of the formula (V) in the Preparations 1, 2 or 3, are deprotected to obtain the compound of the general formula (XX) or a salt thereof. The compound (XX) is then dissolved in a conventional organic solvent such as chloroform, methylene chloride, ethyl acetate or dimethylformamide, and reacted with an acyl chloride of the formula: $R^{10}-CO-Cl$ in the presence of an amine such as triethylamine or pyridine to obtain the compound of the general formula (XXI). In a similar manner, the compound of the general formula (XX) can be reacted with a chloroformate derivative of the formula: $R^{10}-O-CO-Cl$ to obtain the compound of the general formula (XXII), reacted with an isocyanate derivative of the formula: $R^{10}-NCO$ to obtain the compound of the general formula (XXIII), and reacted with a sulfonyl chloride derivative of the formula: $R^{10}-SO_2-Cl$ to obtain the compound of the general formula (XXIV).

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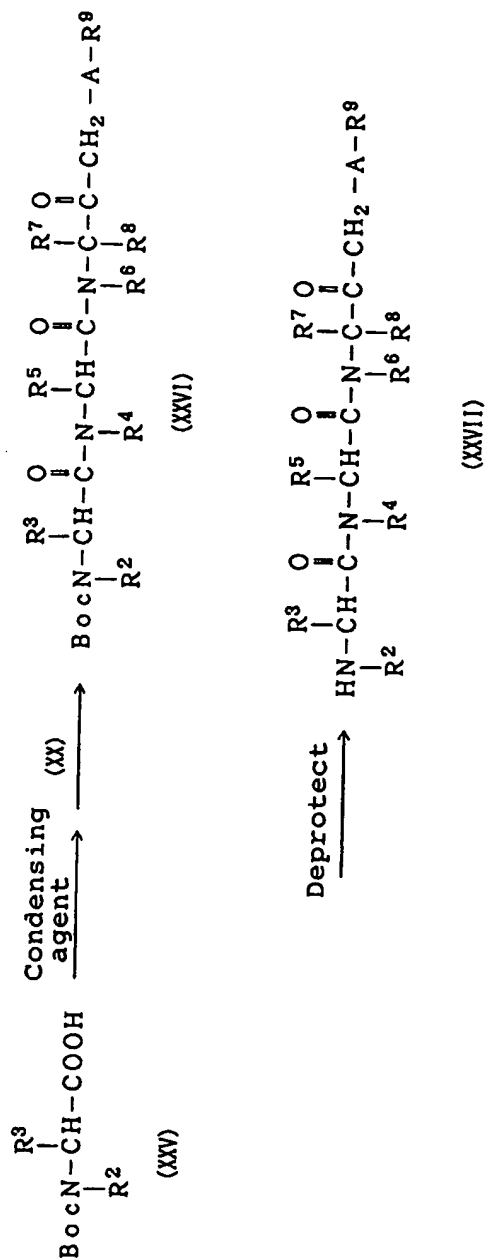
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Preparation 5

[wherein R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 and Boc are as defined above]

In a similar procedure as described in Preparation 1, carboxyl group of an amino acid derivative of the general formula (XXV) is activated with a condensing agent, and the activated amino acid derivative is reacted with the compound (XX) obtained in the above Preparation 4, if necessary, in the presence of a

base to obtain the compound of the general formula (XXVI). The compound (XXVI) can be deprotected in a similar procedure as described in Preparation 1 to obtain the compound of the general formula (XXVII) or a salt thereof. Furthermore, amino group of the compound (XXVII) may be converted according to the procedure described in Preparation 4.

5 Although it may be necessary to protect or deprotect any functional group present on each of the compounds in a series of the procedures in the above-described Preparations 1 to 5, these protection or deprotection can be easily carried out by applying standard methods usually employed in chemistry of organic synthesis.

As will be seen from the results of Experiments below, the compounds (I) of the invention have been
10 proved to possess a potent inhibitory activity against thiol protease such as papain, cathepsin B, cathepsin H, cathepsin L, calpain or the like together with excellent properties regarding oral absorbance, tissue transference and cell membrane permeability, indicating that they are clinically useful in the treatment of various diseases such as muscular dystrophy, amyotrophy, cardiac infarction, stroke, Alzheimer's disease, conscious disturbance and motor disturbance caused by brain trauma, multiple sclerosis, neuropathy of
15 peripheral nerve, cataract, inflammation, allergy, fulminant hepatitis, osteoporosis, hypercalcemia, breast carcinoma, prostatic carcinoma, prostatomegaly or the like, and can be used as cancer growth inhibitors, cancer metastasis preventive agents or platelet-aggregation inhibitors.

When the compounds (I) of the present invention are clinically applied, they can be administered to subjects to be treated after formulating into appropriate forms containing, as an active ingredient, a
20 therapeutically effective amount of compound (I) together with carriers therefor. The appropriate ratio of the active ingredient to the carriers may vary from about 1% by weight to about 90% by weight. For example, the compounds of the present invention may be orally administered after formulating into an appropriate form such as granules, fine granules, powders, tablets, hard capsules, soft capsules, syrups, emulsions, suspensions, solutions or the like. They can be also administered intravenously, intramuscularly or
25 subcutaneously in the form of injections. Furthermore, they may be formulated in the form of suppositories, or powders which are prepared for injections at the time of use.

Formulations of the invention can be prepared using any of known methods in the art. Organic or inorganic, and solid or liquid pharmaceutical carriers or diluents suitable for oral, enteral or parenteral administration may be used for preparing the formulations of the present invention. Examples of excipient
30 usable for preparing solid formulations are lactose, sucrose, starch, talc, cellulose, dextrin, kaolin, calcium carbonate and the like. Liquid formulations for oral administration such as emulsion, syrups, suspensions or solutions generally contain conventional inert diluents such as water or vegetable oils. These formulations may further contain adjuvants such as humectants, suspension aids, edulcorants, aromatics, tinctures or preservatives in addition to the inert diluents. The compound (I) can be formulated into solutions which are
35 filled in absorbable carriers such as hard or soft gelatin capsules. Examples of solvents and suspending agents usable for preparing parenteral formulations such as injections or suppositories are water, propylene glycol, polyethylene glycol, benzyl alcohol, ethyl oleate, lecithin and the like. Examples of the base usable for suppositories are cacao butter, emulsified cacao butter, lauric acid, Witte sol and the like.

The dose of compound (I) may vary depending on various factors such as age, conditions or symptoms
40 of the patient to be treated. Appropriate daily dosage of the compound (I) of the present invention for oral administration to adult is generally about 0.01 - 1000 mg though, it is preferable to adjust appropriately for each case according to the conditions as mentioned above. The daily dosage of the compound (I) may be administered once or in two or three divisions at appropriate intervals or intermittently.

Additionally, when the compound (I) is administered in the form of injections, one dosage of 0.001 - 100
45 mg of said compound can be preferably administered to adult continuously or intermittently.

The following Examples further illustrate the present invention in more detail, but these are illustrative only and are not intended to limit the scope of the invention.

Reference Example 1

50 Preparation of (S)-3-tert-butoxycarbonylamino-1-furfurylthio-2-heptanone

To a solution of (S)-3-tert-butoxycarbonylamino -1-chloro-2-heptanone (6.54 g) and furfurylmercaptan (3.11 g) in tetrahydrofuran (200 ml) was added 2N sodium hydroxide (13 ml), and the mixture was stirred at
55 room temperature for 17 hours. Then, aqueous sodium hydrogencarbonate was added to the mixture, which was extracted with ethyl acetate. The extract was washed with saturated brine, dried over magnesium sulfate and filtered. The filtrate was concentrated and chromatographed on a silica gel column, eluting with hexane containing 10 % ethyl acetate to give the titled product (7.82 g).

Yield: 92%

NMR(CDCl₃, δ): 0.89(t, J=6.6Hz, 3H), 1.20-1.95(m, 6H), 1.44(s, 9H), 3.28(d, J=15Hz, 1H), 3.39(d, J=15Hz, 1H), 3.74(s, 2H), 4.52(m, 1H), 5.09(m, 1H), 6.22(d, J=2.9Hz, 1H), 6.31(m, 1H), 7.36(m, 1H)

5 Reference Example 2

Preparation of (s)-3-amino-1-furfurylthio-2-heptanone hydrochloride

To a solution of (s)-3-tert-butoxycarbonylamino -1-furfurylthio-2-heptanone (7.8 g) obtained in Reference
 10 Example 1 dissolved in ethyl acetate (80 ml) was added 4N hydrogen chloride-containing ethyl acetate
 solution (80 ml), and the mixture was stirred at room temperature for 1 hour. Hexane (100 ml) was then
 added to the mixture. The resultant crystals were filtered, and washed with hexane to give the titled product
 (5.93 g).

Yield: 93%

15 NMR(DMSO-d₆, δ): 0.87(t, J=6.8Hz, 3H), 1.16-1.40(m, 4H), 1.63-1.95(m, 2H), 3.55(d, J=16Hz, 1H), 3.70(d,
 J=16Hz, 1H), 3.81(s, 2H), 4.27(m, 1H), 6.30(m, 1H), 6.41(m, 1H), 7.61(m, 1H), 8.29(m, 3H)

Example 1

20 Preparation of (s)-3-((s)-2-tert-butoxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-2-heptanone
 (compd. No. 43 in Table 1)

(s)-3-Amino-1-furfurylthio-2-heptanone hydrochloride (5.39 g) obtained in Reference Example 2 and (s)-
 tert-butoxycarbonylleucine N-hydroxysuccinimido ester (6.37 g) were dissolved in methylene chloride (150
 25 ml), and triethylamine (5.4 ml) was added to the solution. After the mixture was stirred at room temperature
 for 15 hours, 0.5N aqueous hydrochloric acid (100 ml) was added to the mixture and extracted with
 methylene chloride. The extract was washed with water, saturated aqueous sodium hydrogencarbonate and
 saturated brine sequentially, dried over magnesium sulfate and filtered. The filtrate was concentrated and
 chromatographed on a silica gel column, eluting with hexane containing 25% of ethyl acetate to give the
 30 titled product (8.49 g).

Yield: 96%

IR(neat, cm⁻¹): 3350, 1700, 1675, 1660

NMR(CDCl₃, δ): 0.90-1.0(m, 9H), 1.15-1.75(m, 8H), 1.45(s, 9H), 1.80-1.95(m, 1H), 3.26(d, J=15Hz, 1H), 3.35-
 (d, J=15Hz, 1H), 3.72(s, 2H), 4.14(m, 1H), 4.75(m, 1H), 4.92(d, J=8Hz, 1H), 6.22(d, J=3.1Hz, 1H), 6.30(m,
 35 1H), 6.72(d, J=7Hz, 1H), 7.36(m, 1H)

Example 2

40 Preparation of (s)-3-((s)-2-amino-4-methylvaleryl-amino)-1-furfurylthio-2-heptanone hydrochloride (compd.
 No. 62 in Table 1)

(s)-3-((s)-2-tert-Butoxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-2-heptanone (8.47 g) obtained
 in Example 1 was dissolved in ethyl acetate (25 ml), and 4N hydrogen chloride-containing ethyl acetate
 solution (25 ml) was added to the solution. After the mixture was stirred at room temperature for 50 minutes,
 45 hexane (50 ml) was added to the mixture. Then, the resultant crystals were filtered, and washed with hexane
 to give the titled product (4.31 g).

Yield: 59%

IR(KBr, cm⁻¹): 3300, 1698, 1670

NMR(CD₃OD, δ): 0.88-1.18(m, 9H), 1.27-2.03(m, 9H), 3.41(d, J=15Hz, 1H), 3.50(d, J=15Hz, 1H), 3.79(s,
 50 2H), 3.98(m, 1H), 4.75(dd, J=4.2Hz, 9.3Hz, 1H), 6.28(d, J=3.4Hz, 1H), 6.37(m, 1H), 7.46(m, 1H)

Example 3

55 Preparation of (s)-1-furfurylthio-3-((s)-4-methyl -2-phenoxyacetylaminovaleryl-amino)-2-heptanone (compd.
 No. 82 in Table 1)

(s)-3-((s)-2-Amino-4-methylvaleryl-amino)-1-furfurylthio-2-heptanone hydrochloride (4.31 g) obtained in
 Example 2 was dissolved in methylene chloride (100 ml) and chilled to 0 °C. To the solution were added

phenoxyacetylchloride (2.07 g) and triethylamine (3.2 ml), and the mixture was stirred at 0 °C for 30 minutes, and at room temperature for 30 minutes. Then, 0.5N aqueous hydrochloric acid (50 ml) was added to the mixture, which was extracted with methylene chloride. The extract was washed with water, saturated sodium hydrogencarbonate and saturated brine sequentially, dried over magnesium sulfate and filtered. The filtrate was concentrated, and chromatographed on a silica gel column, eluting with hexane containing 25% ethyl acetate to give the titled product (3.96 g).

Yield: 74%

IR(neat, cm^{-1}): 3300, 1710, 1650

NMR(CDCl_3 , δ): 0.87(t, $J=6.7\text{Hz}$, 3H), 0.93(d, $J=6.0\text{Hz}$, 6H), 1.14-1.40(m, 4H), 1.48-2.0(m, 5H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.53(s, 2H), 4.56(m, 1H), 4.74(m, 1H), 6.23(m, 1H), 6.30(m, 1H), 6.59(d, $J=7\text{Hz}$, 1H), 6.90-7.10(m, 4H), 6.25-6.40(m, 3H)

Example 4

Preparation of (s)-1-furfurylsulfinyl-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-heptanone (compd. No. 83 in Table 1)

(s)-1-Furfurylthio-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-heptanone (176 mg) obtained in Example 3 was dissolved in methanol (10 ml) and water (10 ml). To the solution was added sodium metaperiodate (82 mg), and the mixture was reacted at room temperature for 48 hours. Then, methanol was removed in vacuo, saturated brine was added to the residue, and the resultant mixture was extracted with chloroform. The extract was washed with saturated brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and chromatographed on a silica gel column, eluting with hexane:ethyl acetate (1:1) to give the titled product (66 mg).

Yield: 37%

mp: 96-99 °C

IR(KBr, cm^{-1}): 3320, 1720, 1690, 1650

NMR(CDCl_3 , δ): 0.78-1.07(m, 9H), 1.15-2.05(m, 9H), 3.34-3.70(m, 1H), 4.05-4.78(m, 7H), 6.40(m, 1H), 6.47(m, 1H), 6.80-7.18(m, 5H), 7.20-7.40(m, 2H), 7.43(m, 1H)

Example 5

Preparation of (s)-1-furfurylsulfonyl-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-heptanone (compd. No. 84 in Table 1)

(s)-1-Furfurylthio-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-heptanone (150 mg) obtained in Example 3 was dissolved in methylene chloride (3 ml) and chilled to 0 °C. To the mixture was added metachlorobenzoic acid (177 mg), and the mixture was reacted at 0 °C for 30 minutes, and at room temperature for 10 hours. Then, an aqueous solution of 10% potassium carbonate was added to the mixture, and extracted with methylene chloride. The extract was washed with saturated brine, dried over sodium sulfate, and filtrated. The filtrate was concentrated and chromatographed on a silica gel column, eluting with hexane:ethyl acetate (2:1) to give the titled product (130 mg).

Yield: 80%

mp: 120-121 °C

IR(KBr, cm^{-1}): 3300, 1730, 1650

NMR(CDCl_3 , δ): 0.80-1.0(m, 9H), 1.15-2.05(m, 9H), 3.97(d, $J=15\text{Hz}$, 1H), 4.28(d, $J=15\text{Hz}$, 1H), 4.40-4.63(m, 6H), 6.42(m, 1H), 6.58(m, 1H), 6.82-6.99(m, 4H), 7.04(t, $J=7$, 4Hz, 1H), 7.22-7.40(m, 2H), 7.48(m, 1H)

Example 6

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methyl-valeryl-amino)-1-furfuryloxy -4-phenyl-2-butanone (compd. No. 452 in Table 1)

N-Benzyloxycarbonyl-L-leucyl-L-phenylalanine diazomethylketone (314 mg) was dissolved in furfuryl alcohol (2 ml) and methylene chloride (1 ml). To the solution was added rhodium acetate (II) dimer (10 mg). After the mixture was stirred at room temperature for 1 hour, the solvents was removed in vacuo and the residue was chromatographed on a silica gel column, eluting with hexane-ethyl acetate to give the titled product (27 mg).

Yield: 7.4%

mp: 94-95 °C

IR(KBr, cm⁻¹): 3314, 3285, 1738, 1692, 1653

NMR(CDCl₃, δ): 0.89(d, J=6.0Hz, 6H), 1.35-1.70(m, 3H), 2.94(dd, J=14Hz, 6.2Hz, 1H), 3.10(dd, J=14Hz, 6.5Hz, 1H), 3.97(d, J=17Hz, 1H), 4.12(m, 1H), 4.15(d, J=17Hz, 1H), 4.44(d, J=13Hz, 1H), 4.53(d, J=13Hz, 1H), 4.90-5.05(m, 2H), 5.09(s, 2H), 6.28-6.43(m, 2H), 6.51(d, J=7.0Hz, 1H), 7.08(d, J=7.1Hz, 2H), 7.17-7.30-(m, 3H), 7.35(s, 5H), 7.41(m, 1H)

The compounds in the following Examples were prepared in the same manner as described in Reference Examples 1 and 2 and Examples 1 to 6. Physicochemical properties of each product are shown below.

Example 7

Preparation of 1-((s)-2-benzyloxycarbonylamino)-4-methylvaleryl-amino-3-furfurylthio-2-propanone (compd. No. 2 in Table 1)

mp: 59-62 °C

IR(KBr, cm⁻¹): 3340, 1730, 1692, 1648

NMR(CDCl₃, δ): 0.94(d, J=6.0Hz, 6H), 1.48-1.77(m, 3H), 3.24(s, 2H), 3.72(s, 2H), 4.10-4.35(m, 3H), 4.95-5.11(m, 1H), 5.12(s, 2H), 6.21(d, J=3.1Hz, 1H), 6.32(m, 1H), 6.63(m, 1H), 7.15-7.38(m, 6H)

Example 8

Preparation of 1-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-3-(3-pyridylmethylthio)-2-propanone (compd. No. 5 in Table 1)

IR(neat, cm⁻¹): 3306, 1717, 1666

NMR(CDCl₃, δ): 0.93(d, J=5.8Hz, 6H), 1.42-1.79(m, 3H), 3.10(s, 2H), 3.66(s, 2H), 4.25(d, J=4.7Hz, 2H), 4.28(m, 1H), 5.11(s, 2H), 5.50(d, J=8.2Hz, 1H), 6.93(m, 1H), 7.18-7.42(m, 6H), 7.65(d, J=7.8Hz, 1H), 8.42-8.60(m, 2H)

Example 9

Preparation of 3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-3-methyl-2-butanone (compd. No. 15 in Table 1)

mp: 80-82 °C

IR(KBr, cm⁻¹): 3275, 1728, 1684, 1651

NMR(CDCl₃, δ): 0.92(d, J=5.8Hz, 3H), 0.93(d, J=6.2Hz, 3H), 1.44(s, 3H), 1.46(s, 3H), 1.57-1.77(m, 3H), 3.37(s, 2H), 3.77(s, 2H), 4.13(m, 1H), 5.10(s, 2H), 6.23(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.66(s, 1H), 7.32-7.42-(m, 6H)

Example 10

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-4-methyl-2-pentanone (compd. No. 22 in Table 1)

IR(neat, cm⁻¹): 3300, 1720, 1705, 1660

NMR(CDCl₃, δ): 0.79(d, J=6.8Hz, 3H), 0.92(d, J=6.8Hz, 3H), 0.93(d, J=5.0Hz, 6H), 1.42-1.77(m, 3H), 2.20-(m, 1H), 3.24(d, J=15Hz, 1H), 3.31(d, J=15Hz, 1H), 3.70(s, 2H), 4.25(m, 1H), 4.78(dt, J=8.9Hz, 4.6Hz, 1H), 5.10(s, 2H), 5.39(d, J=7.4Hz, 1H), 6.21(d, J=2.8Hz, 1H), 6.28(m, 1H), 6.73(d, J=8.9Hz, 1H), 7.32(s, 5H), 7.35(m, 1H)

Example 11

Preparation of (s)-1-furfurylthio-4-methyl-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-pentanone (compd. No. 24 in Table 1)

IR(neat, cm^{-1}): 3300, 1720, 1710, 1650

NMR(CDCl_3 , δ): 0.82(d, $J=6.9\text{Hz}$, 3H), 0.91-0.96(m, 9H), 1.49-1.82(m, 3H), 2.23(m, 1H), 3.26(d, $J=15\text{Hz}$, 1H), 3.34(d, $J=15\text{Hz}$, 1H), 3.72(s, 2H), 4.53(s, 2H), 4.60(m, 1H), 4.78(dt, $J=8.8\text{Hz}$, 4.5Hz, 1H), 6.23(d, $J=2.7\text{Hz}$, 1H), 6.30(m, 1H), 6.75(d, $J=8.7\text{Hz}$, 1H), 6.90-6.99(m, 3H), 7.03(m, 1H), 7.25-7.40(m, 3H)

5

Example 12

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino-1-furfurylthio-2-hexanone (compd. No. 28 in Table 1)

10

IR(neat, cm^{-1}): 3350, 1710, 1655

NMR(CDCl_3 , δ): 0.89(t, $J=7.2\text{Hz}$, 3H), 0.94(d, $J=6.2\text{Hz}$, 6H), 1.15-1.95(m, 7H), 3.24(d, $J=15\text{Hz}$, 1H), 3.31(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.21(m, 1H), 4.75(m, 1H), 5.11(s, 2H), 5.21(d, $J=8\text{Hz}$, 1H), 6.22(d, $J=2.9\text{Hz}$, 1H), 6.28(m, 1H), 6.65(m, 1H), 7.30-7.35(m, 6H)

15

Example 13

Preparation of (s)-1-furfurylthio-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-hexanone (compd. No. 30 in Table 1)

20

IR(neat, cm^{-1}): 3300, 1720, 1650

NMR(CDCl_3 , δ): 0.78-1.05(m, 9H), 1.17-1.95(m, 7H), 3.27(d, $J=15\text{Hz}$, 1H), 3.34(d, $J=15\text{Hz}$, 1H), 3.72(s, 2H), 4.53(m, 1H), 4.55(s, 2H), 4.75(m, 1H), 6.23(d, $J=3.0\text{Hz}$, 1H), 6.30(m, 1H), 6.58(d, $J=10\text{Hz}$, 1H), 6.85-7.15(m, 3H), 7.23-7.37(m, 4H)

25

Example 14

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-5-methyl-1-methylthio-2-hexanone (compd. No. 32 in Table 1)

30

mp: 96-97 °C

IR(KBr, cm^{-1}): 3220, 1725, 1693, 1640

NMR(CDCl_3 , δ): 0.93-1.0(m, 12H), 1.35-1.75(m, 6H), 2.06(s, 3H), 3.20(d, $J=14\text{Hz}$, 1H), 3.48(d, $J=14\text{Hz}$, 1H), 4.19(m, 1H), 4.84(m, 1H), 5.11(s, 2H), 5.17(m, 1H), 6.48(d, $J=7\text{Hz}$, 1H), 7.35(s, 5H)

35

Example 15

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio -5-methyl-2-hexanone (compd. No. 35 in Table 1)

40

IR(neat, cm^{-1}): 3300, 1710, 1650

NMR(CDCl_3 , δ): 0.92(d, $J=5.0\text{Hz}$, 6H), 0.94(d, $J=5.0\text{Hz}$, 6H), 1.38-1.79(m, 6H), 3.25(d, $J=15\text{Hz}$, 1H), 3.33(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.19(m, 1H), 4.77(ddd, $J=6.7\text{Hz}$, 6.7Hz, 2.2Hz, 1H), 5.11(s, 2H), 5.15(d, $J=6.7\text{Hz}$, 1H), 6.22(d, $J=2.5\text{Hz}$, 1H), 6.29(m, 1H), 6.49(d, $J=6.7\text{Hz}$, 0.5H), 6.59(d, $J=6.7\text{Hz}$, 0.5H), 7.27-7.40(m, 6H)

45

Example 16

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -2-heptanone (compd. No. 37 in Table 1)

50

mp: 80-82 °C

IR(KBr, cm^{-1}): 3320, 1720, 1685, 1643

NMR(CDCl_3 , δ): 0.83-1.0(m, 9H), 1.18-2.05(m, 9H), 2.07(s, 3H), 3.20(d, $J=14\text{Hz}$, 1H), 3.36(d, $J=14\text{Hz}$, 1H), 4.23(m, 1H), 4.84(m, 1H), 5.12(s, 2H), 5.16(m, 1H), 6.56(d, $J=8\text{Hz}$, 1H), 7.35(s, 5H)

55

Example 17

Preparation of (s)-3-benzyloxycarbonylaminoacetyl amino-1-furfurylthio-2-heptanone (compd. No. 38 in Table 1)

IR(neat, cm^{-1}): 3350, 1720, 1715, 1670

5 NMR(CDCl_3 , δ): 0.87(d, $J=6.7\text{Hz}$, 3H), 1.12-1.40(m, 4H), 1.55(m, 1H), 1.85(m, 1H), 3.26(d, $J=15\text{Hz}$, 1H), 3.34(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 3.90(d, $J=4.3\text{Hz}$, 2H), 4.81(m, 1H), 5.13(s, 2H), 5.54(m, 1H), 6.21(d, $J=3.2\text{Hz}$, 1H), 6.29(m, 1H), 6.72(d, $J=7.0\text{Hz}$, 1H), 7.27-7.41(m, 6H)

Example 18

10

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino propionyl amino)-1-furfurylthio-2-heptanone (compd. No. 39 in Table 1)

mp: 85-87 °C

15 IR(KBr, cm^{-1}): 3300, 1730, 1690, 1660

NMR(CDCl_3 , δ): 0.87(d, $J=6.8\text{Hz}$, 3H), 1.15-1.37(m, 3H), 1.39(d, $J=7.0\text{Hz}$, 3H), 1.45-1.75(m, 2H), 1.87(m, 1H), 3.26(d, $J=15\text{Hz}$, 1H), 3.33(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.26(m, 1H), 4.75(m, 1H), 5.12(s, 2H), 5.32(m, 1H), 6.22(d, $J=3.2\text{Hz}$, 1H), 6.29(m, 1H), 6.61(m, 1H), 7.30-7.36(m, 6H)

20 Example 19

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-3-methylbutyrylamino)-1-furfurylthio-2-heptanone (compd. No. 40 in Table 1)

25 mp: 115-116 °C

IR(KBr, cm^{-1}): 3280, 1715, 1690, 1630

30 NMR(CDCl_3 , δ): 0.86(t, $J=7.0\text{Hz}$, 3H), 0.92(d, $J=6.8\text{Hz}$, 3H), 0.97(d, $J=6.8\text{Hz}$, 3H), 1.15-1.39(m, 4H), 1.53-1.89(m, 1H), 1.89(m, 1H), 2.14(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.02(dt, $J=8.2\text{Hz}$, 6.1Hz, 1H), 4.78(m, 1H), 5.11(s, 2H), 5.38(d, $J=8.2\text{Hz}$, 1H), 6.21(d, $J=2.6\text{Hz}$, 1H), 6.29(m, 1H), 6.56(d, $J=7.7\text{Hz}$, 1H), 7.27-7.42(m, 6H)

Example 20

35 Preparation of (s)-3-((s)-2-benzyloxycarbonylaminovaleryl amino)-1-furfurylthio-2-heptanone (compd. No. 41 in Table 1)

mp: 95-96 °C

IR(KBr, cm^{-1}): 3280, 3260, 1690, 1680, 1640

40 NMR(CDCl_3 , δ): 0.86(t, $J=7.0\text{Hz}$, 3H), 0.93(t, $J=7.2\text{Hz}$, 3H), 1.16-1.47(m, 6H), 1.50-1.67(m, 2H), 1.75-1.97-3.27(d, $J=15\text{Hz}$, 1H), 3.33(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.19(m, 1H), 4.77(m, 2H), 5.11(s, 2H), 5.30-6.21(d, $J=7.1\text{Hz}$, 1H), 6.21(d, $J=3.1\text{Hz}$, 1H), 6.30(m, 1H), 6.59(d, $J=7.1\text{Hz}$, 1H), 7.37-7.43(m, 6H)

Example 21

45 Preparation of (s)-3-((s)-2-cyclohexylmethoxycarbonylamino-4-methylvaleryl amino)-1-furfurylthio-2-heptanone (compd. No. 46 in Table 1)

IR(neat, cm^{-1}): 3330, 1715, 1660

50 NMR(CDCl_3 , δ): 0.93(t, $J=6.9\text{Hz}$, 3H), 0.94(d, $J=3.9\text{Hz}$, 6H), 1.10-2.0(m, 20H), 3.26(d, $J=15\text{Hz}$, 1H), 3.34(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 3.87(d, $J=6.4\text{Hz}$, 2H), 4.13(m, 1H), 4.74(m, 1H), 5.0(d, $J=6.4\text{Hz}$, 1H), 6.21(d, $J=2.6\text{Hz}$, 1H), 6.29(m, 1H), 6.60(d, $J=8\text{Hz}$, 1H), 7.35(m, 1H)

Example 22

55 Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl amino)-1-furfurylthio-2-heptanone (compd. No. 48 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1655

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NMR(CDCl₃, δ): 0.87(t, J = 6.8Hz, 3H), 0.95(d, J = 5.9Hz, 6H), 1.15-2.0(m, 9H), 3.26(d, J = 14Hz, 1H), 3.33(d, J = 14Hz, 1H), 3.72(s, 2H), 4.20(m, 1H), 4.75(m, 1H), 5.12(s, 2H), 5.13(m, 1H), 6.22(m, 1H), 6.30(m, 1H), 6.55(d, J = 7Hz, 1H), 7.26-7.45(m, 6H)

5 Example 23

Preparation of (s)-3-[(s)-2-(2-fluorobenzyloxycarbonylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 49 in Table 1)

10 IR(neat, cm⁻¹): 3320, 1710, 1655

NMR(CDCl₃, δ): 0.87(t, J = 5.8Hz, 3H), 0.94(d, J = 5.6Hz, 6H), 1.07-2.0(m, 9H), 3.25(d, J = 14Hz, 1H), 3.32(d, J = 14Hz, 1H), 3.71(s, 2H), 4.13(m, 1H), 4.75(m, 1H), 5.05-5.27(m, 3H), 6, 22(m, 1H), 6, 29(m, 1H), 6.53(d, J = 9Hz, 1H), 6.98-7.19(m, 2H), 7.21-7.43(m, 3H)

15 Example 24

Preparation of (s)-3-[(s)-2-(4-fluorobenzyloxycarbonylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 51 in Table 1)

20 mp: 67-68 ° C

IR(KBr, cm⁻¹): 3400, 3250, 1725, 1640

NMR(CDCl₃, δ): 0.87(t, J = 7.2Hz, 3H), 0.94(d, J = 5.0Hz, 6H), 1.10-2.0(m, 9H), 3.27(d, J = 14Hz, 1H), 3.37(d, J = 14Hz, 1H), 3.71(s, 2H), 4.17(m, 1H), 4.76(m, 1H), 5.07(s, 2H), 5.15(d, J = 7Hz, 1H), 6.22(d, J = 2.9Hz, 1H), 6, 30(m, 1H), 6, 50(d, J = 7Hz, 1H), 7.05(t, J = 8.6Hz, 2H), 7.30-7.45(m, 3H)

25

Example 25

Preparation of (s)-3-[(s)-2-(2-cyanobenzyloxycarbonylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 56 in Table 1)

30

IR(neat, cm⁻¹): 3281, 1766, 1712, 1658

NMR(CDCl₃, δ): 0.85-1.06(m, 9H), 1.25-1.43(m, 4H), 1.52-1.83(m, 3H), 1.83-2.02(m, 2H), 3.24(d, J = 15Hz, 1H), 3.33(d, J = 15Hz, 1H), 3.67(s, 2H), 4.56(m, 1H), 4.77(m, 1H), 5.33(s, 2H), 6.17(d, J = 3.1Hz, 1H), 6.23(m, 1H), 6, 25(d, J = 8.3Hz, 1H), 7.28(dd, J = 6.4Hz, 5.3Hz, 1H), 7.36(m, 1H), 7.43-7.65(m, 3H), 7.90(d, J = 7.3Hz, 1H)

35

Example 26

Preparation of (s)-3-[(s)-2-(3-cyanobenzyloxycarbonylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 57 in Table 1)

40

IR(KBr, cm⁻¹): 3400, 3250, 2220, 1710, 1630

NMR(CDCl₃, δ): 0.87(t, J = 6.6Hz, 3H), 0.95(d, J = 5.3Hz, 6H), 1.09-1.39(m, 4H), 1.42-1.77(m, 4H), 1.89(m, 1H), 3.26(d, J = 15Hz, 1H), 3.34(d, J = 15Hz, 1H), 3.71(s, 2H), 4.19(m, 1H), 4.77(m, 1H), 5.13(s, 2H), 5.25(d, J = 7.8Hz, 1H), 6.21(d, J = 3.1Hz, 1H), 6.30(m, 1H), 6.61(d, J = 7.3Hz, 1H), 7.26(s, 1H), 7.35(m, 1H), 7.45(m, 1H), 7.51-7.63(m, 2H)

45

Example 27

Preparation of (s)-3-[(s)-2-(4-cyanobenzyloxycarbonylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 58 in Table 1)

50

mp: 83-89 ° C

IR(KBr, cm⁻¹): 3400, 3270, 2220, 1720, 1700, 1640

55

NMR(CDCl₃, δ): 0.86(t, J = 7.0Hz, 3H), 0.95(d, J = 6.2Hz, 6H), 1.13-1.40(m, 3H), 1.43-1.79(m, 5H), 1.79-1.99(m, 1H), 3.26(d, J = 15Hz, 1H), 3.30(d, J = 15Hz, 1H), 3.72(s, 2H), 4.19(m, 1H), 4.77(m, 1H), 5.16(s, 2H), 5.32(d, J = 8.0Hz, 1H), 6.21(d, J = 2.9Hz, 1H), 6.30(m, 1H), 6.55(d, J = 7.6Hz, 1H), 7.36(m, 1H), 7.44(d, J = 8.3Hz, 2H), 7.65(d, J = 8.3Hz, 2H)

Example 28

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2-pyridylmethoxycarbonylamino)valeryl-amino]-2-heptanone (compd. No. 59 in Table 1)

IR(neat, cm^{-1}): 3350, 1715, 1660

NMR(CDCl_3 , δ): 0.86(t, $J=6.7\text{Hz}$, 3H), 0.95(d, $J=3.8\text{Hz}$, 6H), 1.07-1.99(m, 9H), 3.27(d, $J=15\text{Hz}$, 1H), 3.32(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.22(m, 1H), 4.77(m, 1H), 5.24(s, 2H), 5.32(d, $J=8\text{Hz}$, 1H), 6.21(d, $J=3.2\text{Hz}$, 1H), 6.29(m, 1H), 6.63(d, $J=7\text{Hz}$, 1H), 7.20-7.40(m, 3H), 7.69(m, 1H), 8.58(d, $J=3.1\text{Hz}$, 1H)

Example 29

Preparation of (s)-3-[(s)-2-cyclohexylcarbonylamino-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 65 in Table 1)

mp: 109°C(dec.)

IR(KBr, cm^{-1}): 3294, 1707, 1637

NMR(CDCl_3 , δ): 0.87(t, $J=7.0\text{Hz}$, 3H), 0.98(d, $J=6.7\text{Hz}$, 3H), 0.99(d, $J=6.7\text{Hz}$, 3H), 1.11-1.75(m, 13H), 1.75-1.99(m, 6H), 2.10(m, 1H), 3.26(d, $J=15\text{Hz}$, 1H), 3.30(d, $J=15\text{Hz}$, 1H), 3.72(s, 2H), 4.47(m, 1H), 4.71(m, 1H), 5.90(d, $J=8.1\text{Hz}$, 1H), 6.21(d, $J=2.6\text{Hz}$, 1H), 6.30(m, 1H), 6.81(d, $J=7.6\text{Hz}$, 1H), 7.36(m, 1H)

Example 30

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-phenylacetylaminovale-rylamino]-2-heptanone (compd. No. 66 in Table 1)

IR(neat, cm^{-1}): 3260, 1710, 1635

NMR(CDCl_3 , δ): 0.75-1.07(m, 9H), 1.13-1.99(m, 9H), 3.20-3.38(m, 2H), 3.59(s, 2H), 3.71(s, 2H), 4.43(m, 1H), 4.68(m, 1H), 5.78(d, $J=8\text{Hz}$, 1H), 6.21(d, $J=3.2\text{Hz}$, 1H), 6.29(m, 1H), 6.62(d, $J=7.4\text{Hz}$, 1H), 7.16-7.40(m, 6H)

Example 31

Preparation of (s)-3-[(s)-2-(4-fluorophenylacetylaminovale-rylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 69 in Table 1)

IR(neat, cm^{-1}): 3300, 1715, 1660, 1640

NMR(CDCl_3 , δ): 0.76-0.97(m, 9H), 1.07-1.96(m, 9H), 3.20-3.35(m, 2H), 3.55(d, $J=4.3\text{Hz}$, 2H), 3.71(s, 2H), 4.46(m, 1H), 4.71(m, 1H), 5.85(d, $J=7\text{Hz}$, 1H), 6.20(d, $J=3.0\text{Hz}$, 1H), 6.29(m, 1H), 6.59(d, $J=6\text{Hz}$, 0.6H), 6.69(d, $J=6\text{Hz}$, 0.4H), 7.03(t, $J=8.6\text{Hz}$, 2H), 7.17-7.35(m, 3H)

Example 32

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2,3-methylenedioxyphenylacetylaminovale-rylamino)-2-heptanone (compd. No. 73 in Table 1)

IR(neat, cm^{-1}): 3280, 1720, 1640

NMR(CDCl_3 , δ): 0.80-1.0(m, 9H), 1.13-1.98(m, 9H), 3.20-3.37(m, 2H), 3.55(d, $J=3.9\text{Hz}$, 2H), 3.71(s, 2H), 4.44(m, 1H), 4.70(m, 1H), 5.90-6.07(m, 3H), 6.21(d, $J=3.1\text{Hz}$, 1H), 6.29(m, 1H), 6.65(d, $J=7\text{Hz}$, 1H), 6.70-6.93(m, 3H), 7.35(m, 1H)

Example 33

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(1-naphthylacetylaminovale-rylamino)-2-heptanone (compd. No. 76 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1640

NMR(CDCl_3 , δ): 0.70(d, $J=6.5\text{Hz}$, 3H), 0.72(d, $J=6.5\text{Hz}$, 3H), 0.85(t, $J=7.2\text{Hz}$, 3H), 1.05-1.91(m, 9H), 3.20-

3.38(m, 2H), 3.70(s, 2H), 4.02(d, J=11Hz, 1H), 4.10(d, J=11Hz, 1H), 4.39(m, 1H), 4.63(m, 1H), 5.59(d, J=8Hz, 1H), 6.21(d, J=2.9Hz, 1H), 6.36(m, 1H), 6.55(d, J=7Hz, 0.5H), 6.62(d, J=7Hz, 0.5H), 7.30-7.61(m, 5H), 7.80-8.0(m, 3H)

5 Example 34

Preparation of (s)-3-[(s)-2-(3-benzothiénylacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 79 in Table 1)

IR(neat, cm⁻¹): 3300, 1715, 1640

10 NMR(CDCl₃, δ): 0.71-1.0(m, 9H), 1.07-1.97(m, 9H), 3.24(d, J=3.7Hz, 0.7H), 3.27(d, J=3.0Hz, 1.3H), 3.70(s, 1.3H), 3.71(s, 0.7H), 3.84(s, 1.3H), 3.85(s, 0.7H), 4.40(m, 1H), 4.67(m, 1H), 5.91(m, 1H), 6.20(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.57(d, J=6Hz, 0.7H), 6.70(d, J=6Hz, 0.3H), 7.34-7.45(m, 4H), 7.71(m, 1H), 7.87(m, 1H)

Example 35

15

Preparation of (s)-3-[(s)-2-(cyclohexyloxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 81 in Table 1)

IR(neat, cm⁻¹): 3400, 3300, 1715, 1665

20 NMR(CDCl₃, δ): 0.80-1.0(m, 11H), 1.10-1.99(m, 17H), 3.29-3.40(m, 3H), 3.71(s, 0.7H), 3.72(s, 1.3H), 3.98(d, J=1.0Hz, 1.3H), 3.99(s, 0.7H), 4.50(m, 1H), 4.74(m, 1H), 6.22(d, J=2.7Hz, 1H), 6.30(m, 1H), 6.70(d, J=7Hz, 0.7H), 6.77(d, J=7Hz, 0.3H), 6.92(d, J=8Hz, 1H), 7.35(m, 1H)

Example 36

25

Preparation of (s)-3-[(s)-2-(2-fluorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 85 in Table 1)

mp: 60-62 °C

30 IR(KBr, cm⁻¹): 3340, 1715, 1670, 1640

NMR(CDCl₃, δ): 0.87(t, J=7.0Hz, 3H), 0.95(d, J=6.1Hz, 6H), 1.10-1.99(m, 9H), 3.26(d, J=15Hz, 1H), 3.34(d, J=15Hz, 1H), 3.72(s, 2H), 4.53(m, 1H), 4.57(s, 2H), 4.75(m, 1H), 6.22(d, J=2.8Hz, 1H), 6.29(m, 1H), 6.65(d, J=8Hz, 1H), 6.90-7.20(m, 5H), 7.36(m, 1H)

35 Example 37

Preparation of (s)-3-[(s)-2-(3-fluorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 86 in Table 1)

40 IR(neat, cm⁻¹): 3300, 1750, 1650

NMR(CDCl₃, δ): 0.87(t, J=7.2Hz, 3H), 0.93(d, J=6.3Hz, 6H), 1.15-2.0(m, 9H), 3.20-3.40(m, 2H), 3.71(d, J=6.4Hz, 2H), 4.51(d, J=2.2Hz, 2H), 4.61(m, 1H), 4.76(m, 1H), 6.21(d, J=3.1Hz, 1H), 6.28(m, 1H), 6.62-6.79(m, 3H), 6.81-7.10(m, 2H), 7.18-7.39(m, 2H)

45 Example 38

Preparation of (s)-3-[(s)-2-(4-fluorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 87 in Table 1)

50 mp: 88-91 °C

IR(KBr, cm⁻¹): 3300, 1700, 1640

NMR(CDCl₃, δ): 0.86(t, J=7.0Hz, 3H), 0.93(d, J=5.7Hz, 6H), 1.10-2.0(m, 9H), 3.21-3.32(m, 2H), 3.71(d, J=5.6Hz, 2H), 4.48(d, J=2.7Hz, 2H), 4.59(m, 1H), 4.76(m, 1H), 6.20(d, J=3.1Hz, 1H), 6.27(m, 1H), 6.65(m, 1H), 6.78-7.10(m, 5H), 7.30-7.42(m, 1H)

55

Example 39

Preparation of (s)-3-[(s)-2-(2-chlorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone

(compd. No. 88 in Table 1)

IR(neat, cm^{-1}): 3320, 1715, 1650

5 NMR(CDCl_3 , δ): 0.85(t, $J=3.9\text{Hz}$, 3H), 0.92-1.05(m, 6H), 1.15-1.98(m, 9H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 4.54(s, 2H), 4.52(m, 1H), 4.75(m, 1H), 6.22(m, 1H), 6.29(m, 1H), 6.79-7.05(m, 3H), 7.17-7.31(m, 2H), 7.33-7.45(m, 2H)

Example 40

10 Preparation of (s)-3-[(s)-2-(4-chlorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 90 in Table 1)

mp: 66-67°C

IR(KBr, cm^{-1}): 3320, 1710, 1645

15 NMR(CDCl_3 , δ): 0.87(t, $J=6.9\text{Hz}$, 3H), 0.92(d, $J=7.4\text{Hz}$, 6H), 1.07-1.99(m, 9H), 3.23-3.38(m, 2H), 3.72(d, $J=5.0\text{Hz}$, 2H), 4.50(d, $J=3.2\text{Hz}$, 2H), 4.53(m, 1H), 4.76(m, 1H), 6.20(m, 1H), 6.28(m, 1H), 6.57(d, $J=8\text{Hz}$, 0.5H), 6.70(d, $J=8\text{Hz}$, 0.5H), 6.79-6.99(m, 4H), 7.29(d, $J=1.5\text{Hz}$, 1H), 7.36(m, 1H)

Example 41

20 Preparation of (s)-3-[(s)-2-(2,3-dichlorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 91 in Table 1)

mp: 79-80°C

25 IR(KBr, cm^{-1}): 3300, 1715, 1660, 1645

NMR(CDCl_3 , δ): 0.87(t, $J=7.0\text{Hz}$, 3H), 0.94(d, $J=5.2\text{Hz}$, 3H), 0.96(d, $J=5.5\text{Hz}$, 3H), 1.10-2.0(m, 9H), 3.23-3.40(m, 2H), 3.72(d, $J=3.6\text{Hz}$, 2H), 4.51(m, 1H), 4.57(s, 2H), 4.75(m, 1H), 6.21(m, 1H), 6.29(m, 1H), 6.58(d, $J=7\text{Hz}$, 0.7H), 6.70(d, $J=7\text{Hz}$, 0.3H), 6.82(m, 1H), 7.10-7.22(m, 3H), 7.35(d, $J=1.9\text{Hz}$, 1H)

30 Example 42

Preparation of (s)-3-[(s)-2-(2,4-dichlorophenoxyacetyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 92 in Table 1)

35 mp: 107-108°C

IR(KBr, cm^{-1}): 3300, 1715, 1660, 1640

NMR(CDCl_3 , δ): 0.87(t, $J=7.1\text{Hz}$, 3H), 0.93-0.98(m, 6H), 1.05-1.99(m, 9H), 3.27(d, $J=14\text{Hz}$, 1H), 3.36(d, $J=14\text{Hz}$, 1H), 3.70(s, 0.4H), 3.72(s, 1.6H), 4.52(m, 1H), 4.54(s, 2H), 4.78(m, 1H), 6.21(d, $J=3.1\text{Hz}$, 1H), 6.30(m, 1H), 6.58(d, $J=7\text{Hz}$, 0.8H), 6.70(d, $J=7\text{Hz}$, 0.2H), 6.84(d, $J=9\text{Hz}$, 1H), 7.08-7.50(m, 4H)

40

Example 43

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2,4,6-trichlorophenoxyacetyl-amino)valeryl-amino]-2-heptanone (compd. No. 94 in Table 1)

45

IR(neat, cm^{-1}): 3300, 1710, 1640

NMR(CDCl_3 , δ): 0.82-0.89(m, 3H), 0.92-1.10(m, 6H), 1.17-2.0(m, 9H), 3.22-3.40(m, 2H), 3.70(s, 0.4H), 3.72(s, 1.6H), 4.51(d, $J=1.6\text{Hz}$, 2H), 4.63(m, 1H), 4.76(m, 1H), 6.21(d, $J=2.6\text{Hz}$, 1H), 6.28(m, 1H), 6.83(d, $J=7\text{Hz}$, 0.8H), 6.92(d, $J=7\text{Hz}$, 0.2H), 7.23-7.40(m, 4H)

50

Example 44

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2-methylphenoxyacetyl-amino)valeryl-amino]-2-heptanone (compd. No. 96 in Table 1)

55

IR(neat, cm^{-1}): 3300, 1710, 1650

NMR(CDCl_3 , δ): 0.87(t, $J=6.9\text{Hz}$, 3H), 0.94(d, $J=6.1\text{Hz}$, 6H), 1.07-1.97(m, 9H), 2.30(s, 3H), 3.19-3.39(m, 2H), 3.71(d, $J=4.6\text{Hz}$, 2H), 4.53(d, $J=1.8\text{Hz}$, 2H), 4.54(m, 1H), 4.76(m, 1H), 6.22(m, 1H), 6.30(m, 1H), 6.55-

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6.82(m, 2H), 6.87-7.03(m, 2H), 7.11-7.21(m, 2H), 7.30-7.40(m, 1H)

Example 45

- 5 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(3-methylphenoxyacetyl amino)valeryl amino]-2-heptanone (compd. No. 97 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1650

- 10 NMR(CDCl_3 , δ): 0.78-1.01(m, 9H), 1.05-1.95(m, 9H), 2.33(s, 3H), 3.21-3.38(m, 2H), 3.70(s, 1.3H), 3.72(s, 0.7H), 4.50(s, 0.7H), 4.51(s, 1.3H), 4.56(m, 1H), 4.73(m, 1H), 6.20(m, 1H), 6.28(m, 1H), 6.58-6.80(m, 3H), 6.84(d, $J=6.9\text{Hz}$, 1H), 6.92(d, $J=8.3\text{Hz}$, 1H), 7.19(t, $J=7.7\text{Hz}$, 1H), 7.35(m, 1H)

Example 46

- 15 Preparation of (s)-3-[(s)-2-(4-chloro-2-methylphenoxyacetyl amino)-4-methylvaleryl amino]-1-furfurylthio-2-heptanone (compd. No. 100 in Table 1)

IR(neat, cm^{-1}): 3300, 1715, 1650

- 20 NMR(CDCl_3 , δ): 0.86(t, $J=7.0\text{Hz}$, 3H), 0.95(d, $J=5.3\text{Hz}$, 6H), 1.19-1.99(m, 9H), 2.25(s, 3H), 3.22-3.38(m, 2H), 3.71(d, $J=5.9\text{Hz}$, 2H), 4.49(s, 2H), 4.60(q, $J=7.6\text{Hz}$, 1H), 4.78(m, 1H), 6.20(m, 1H), 6.27(m, 1H), 6.63-6.80(m, 1.5H), 6.82-7.20(m, 3.5H), 7.35(m, 1H)

Example 47

- 25 Preparation of (s)-1-furfurylthio-3-[(s)-2-(2-methoxyphenoxyacetyl amino)-4-methylvaleryl amino]-2-heptanone (compd. No. 102 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1650

- 30 NMR(CDCl_3 , δ): 0.85(t, $J=7.1\text{Hz}$, 3H), 0.91(d, $J=6.2\text{Hz}$, 3H), 0.93(d, $J=6.2\text{Hz}$, 3H), 1.07-1.37(m, 5H), 1.42-1.63(m, 2H), 1.63-1.95(m, 2H), 3.25(d, $J=15\text{Hz}$, 1H), 3.33(d, $J=15\text{Hz}$, 1H), 3.71(s, 2H), 3.88(s, 3H), 4.50(m, 1H), 4.56(s, 2H), 4.70(m, 1H), 6.22(d, $J=2.9\text{Hz}$, 1H), 6.30(m, 1H), 6.74(d, $J=7.6\text{Hz}$, 1H), 6.84-7.0(m, 3H), 7.05(m, 1H), 7.35(m, 1H), 7.47(d, $J=8.0\text{Hz}$, 1H)

Example 48

- 35 Preparation of (s)-1-furfurylthio-3-[(s)-2-(4-methoxyphenoxyacetyl amino)-4-methylvaleryl amino]-2-heptanone (compd. No. 104 in Table 1)

mp: 86-88° C

- 40 IR(KBr, cm^{-1}): 3302, 3261, 1712, 1668, 1637
NMR(CDCl_3 , δ): 0.86(t, $J=6.9\text{Hz}$, 3H), 0.94(d, $J=6.0\text{Hz}$, 6H), 1.17-1.39(m, 4H), 1.45-1.78(m, 4H), 1.89(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 3.77(s, 3H), 4.43(d, $J=10\text{Hz}$, 1H), 4.48(d, $J=10\text{Hz}$, 1H), 4.61(m, 1H), 4.74(m, 1H), 6.22(d, $J=3.1\text{Hz}$, 1H), 6.30(m, 1H), 6.80-6.91(m, 5H), 7.01(d, $J=8.4\text{Hz}$, 1H), 7.36(m, 1H)

Example 49

- 50 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-phenylthioacetyl amino]valeryl amino]-2-heptanone (compd. No. 107 in Table 1)

IR(neat, cm^{-1}): 3300, 1715, 1640

- 55 NMR(CDCl_3 , δ): 0.78-1.05(m, 9H), 1.15-2.05(m, 9H), 3.18-3.27(m, 2H), 3.57-3.75(m, 4H), 4.50(m, 1H), 4.69(m, 1H), 6.21(d, $J=2.4\text{Hz}$, 1H), 6.29(m, 1H), 6.68(d, $J=8\text{Hz}$, 0.4H), 6.81(d, $J=8\text{Hz}$, 0.6H), 7.08-7.40(m, 7H)

Example 50

- Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(3-phenoxypropionyl amino)valeryl amino]-2-heptanone (compd. No. 109 in Table 1)

IR(neat, cm^{-1}): 3300, 1715, 1640

NMR(CDCl_3 , δ): 0.83(t, $J=6.8\text{Hz}$, 3H), 0.90-0.94(m, 6H), 1.10-1.99(m, 9H), 2.66(t, $J=5.9\text{Hz}$, 1H), 2.69(t, $J=5.9\text{Hz}$, 1H), 3.20-3.38(m, 2H), 3.68(s, 1.3H), 3.70(s, 0.7H), 4.25(t, $J=5.9\text{Hz}$, 2H), 4.55(m, 1H), 4.70(m, 1H), 6.20(d, $J=3.3\text{Hz}$, 1H), 6.28(m, 1H), 6.52(d, $J=7\text{Hz}$, 1H), 6.80-7.01(m, 4H), 7.20-7.40(m, 3H)

5

Example 51

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(5,6,7,8-tetrahydro-1-naphthoxyacetyl amino) valeryl amino]-2-heptanone (compd. No. 111 in Table 1)

10

NMR(CDCl_3 , δ): 0.80-1.08(m, 9H), 1.15-2.0(m, 13H), 2.67-2.80(m, 4H), 3.21-3.40(m, 2H), 3.71(d, $J=7.3\text{Hz}$, 2H), 4.49(s, 2H), 4.60(m, 1H), 4.76(q, $J=4.6\text{Hz}$, 1H), 6.20(m, 1H), 6.27(m, 1H), 6.58(d, $J=8\text{Hz}$, 1H), 6.70-6.85(m, 2H), 6.87-7.10(m, 2H), 7.35(m, 1H)

15

Example 52

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(1-naphthoxyacetyl amino)valeryl amino]-2-heptanone (compd. No. 114 in Table 1)

20

IR(neat, cm^{-1}): 3300, 1710, 1650

NMR(CDCl_3 , δ): 0.80-0.98(m, 9H), 1.10-2.0(m, 9H), 3.28(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.58(m, 1H), 4.73(s, 2H), 4.74(m, 1H), 6.22(m, 1H), 6.29(m, 1H), 6.63(d, $J=7\text{Hz}$, 1H), 6.83(d, $J=7\text{Hz}$, 1H), 7.01(d, $J=7.1\text{Hz}$, 1H), 7.32-7.60(m, 5H), 7.83(m, 1H), 8.21(m, 1H)

25

Example 53

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2-naphthoxyacetyl amino)valeryl amino]-2-heptanone (compd. No. 115 in Table 1)

30

mp: 87-89 °C

IR(KBr, cm^{-1}): 3270, 1700, 1665, 1640

NMR(CDCl_3 , δ): 0.78-1.0(m, 9H), 1.05-1.98(m, 9H), 3.21-3.40(m, 2H), 3.69(s, 0.2H), 3.72(s, 1.8H), 4.50-4.70(m, 1H), 4.62(s, 2H), 4.74(m, 1H), 6, 22(d, $J=3.1\text{Hz}$, 1H), 6.29(m, 1H), 6.67(d, $J=9\text{Hz}$, 0.9H), 6.80(d, $J=9\text{Hz}$, 0.1H), 6.97(d, $J=9\text{Hz}$, 1H), 7.12-7.93(m, 8H)

35

Example 54

Preparation of (s)-3-[(s)-2-benzoylamino-4-methylvaleryl amino]-1-furfurylthio-2-heptanone (compd. No. 116 in Table 1)

40

IR(neat, cm^{-1}): 3300, 1710, 1630

NMR(CDCl_3 , δ): 0.83(t, $J=6.7\text{Hz}$, 1.5H), 0.89(t, $J=6.7\text{Hz}$, 1.5H), 1.01(d, $J=5.8\text{Hz}$, 6H), 1.15-2.0(m, 9H), 3.28(d, $J=15\text{Hz}$, 0.5H), 3.30(d, $J=15\text{Hz}$, 0.5H), 3.36(d, $J=15\text{Hz}$, 0.5H), 3.38(d, $J=15\text{Hz}$, 0.5H), 3.71(s, 1H), 3.75(s, 1H), 4.69-4.84(m, 2H), 6.21(d, $J=2.5\text{Hz}$, 0.5H), 6.24(d, $J=2.5\text{Hz}$, 0.5H), 6.29(m, 0.5H), 6.33(m, 0.5H), 45 6.61(d, $J=7\text{Hz}$, 1H), 6.76(d, $J=7\text{Hz}$, 0.5H), 6.82(d, $J=7\text{Hz}$, 0.5H), 7.24-7.87(m, 6H)

Example 55

Preparation of (s)-3-[(s)-2-(2-fluorobenzoylamino)-4-methylvaleryl amino]-1-furfurylthio -2-heptanone (compd. No. 117 in Table 1)

50

mp: 102-103 °C

IR(KBr, cm^{-1}): 3287, 1734, 1635

NMR(CDCl_3 , δ): 0.81(t, $J=6.7\text{Hz}$, 3H), 0.97(d, $J=5.6\text{Hz}$, 3H), 0.99(d, $J=5.7\text{Hz}$, 3H), 1.15-1.40(m, 4H), 1.51-1.65(m, 1H), 1.65-1.82(m, 3H), 1.90(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.72(s, 1H), 4.63-4.82(m, 2H), 6.23(d, $J=3.2\text{Hz}$, 1H), 6.30(m, 1H), 6.74(d, $J=7.4\text{Hz}$, 1H), 7.04(dd, $J=9.0\text{Hz}$, 7.6Hz, 1H), 7.12-(dd, $J=12\text{Hz}$, 8.3Hz, 1H), 7.27(d, $J=12\text{Hz}$, 1H), 7.36(m, 1H), 7.48(m, 1H), 8.07(ddd, $J=7.8\text{Hz}$, 7.8Hz, 1.7Hz, 1H)

55

Example 56

Preparation of (s)-3-[(s)-2-(3-fluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio -2-heptanone (compd. No. 118 in Table 1)

IR(KBr, cm^{-1}): 3285, 1734, 1635

NMR(CDCl_3 , δ): 0.79(t, J=6.7Hz, 3H), 0.94(d, J=5.0Hz, 6H), 1.13-1.38(m, 4H), 1.43-1.63(m, 1H), 1.64-1.97-(m, 4H), 3.34(s, 2H), 3.72(s, 2H), 4.71(m, 1H), 4.85(m, 1H), 6.22(d, J=3.1Hz, 1H), 6.29(m, 1H), 7.16(ddd, J=8.3Hz, 8.3Hz, 2.4Hz, 1H), 7.28-7.45(m, 3H), 7.50-7.62(m, 3H)

Example 57

Preparation of (s)-3-[(s)-2-(4-fluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio -2-heptanone (compd. No. 119 in Table 1)

IR(KBr, cm^{-1}): 3315, 1716, 1637

NMR(CDCl_3 , δ): 0.81(t, J=6.6Hz, 3H), 0.98(d, J=5.5Hz, 6H), 1.17-1.39(m, 4H), 1.57(m, 1H), 1.62-1.82(m, 3H), 1.89(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 4.65-4.87(m, 2H), 6.22(d, J=3.1Hz, 1H), 6.30(m, 1H), 6.67(d, J=7.7Hz, 1H), 6.75(d, J=7.7Hz, 1H), 7.11(dd, J=8.7Hz, 8.7Hz, 2H), 7.36(m, 1H), 7.75-7.84(m, 2H)

Example 58

Preparation of (s)-3-[(s)-2-(2,3-difluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 120 in Table 1)

mp: 120-122 °C

IR(KBr, cm^{-1}): 3285, 1734, 1658, 1635

NMR(CDCl_3 , δ): 0.82(t, J=6.6Hz, 3H), 0.98(d, J=6.0Hz, 3H), 0.99(d, J=6.2Hz, 3H), 1.15-1.39(m, 4H), 1.56-(m, 1H), 1.63-1.82(m, 3H), 1.90(m, 1H), 3.27(d, J=15Hz, 1H), 3.30(d, J=15Hz, 1H), 3.72(s, 2H), 4.68(m, 1H), 4.76(m, 1H), 6.23(d, J=3.1Hz, 1H), 6.30(m, 1H), 6.64(d, J=7.4Hz, 1H), 6.92(d, J=11Hz, 0.5H), 6.96(d, J=11Hz, 0.5H), 7.17-7.40(m, 4H)

Example 59

Preparation of (s)-3-[(s)-2-(2,4-difluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 121 in Table 1)

mp: 97-98 °C

IR(KBr, cm^{-1}): 3283, 1730, 1658, 1633

NMR(CDCl_3 , δ): 0.82(t, J=6.7Hz, 3H), 0.97(d, J=6.1Hz, 3H), 0.99(d, J=6.1Hz, 3H), 1.17-1.39(m, 4H), 1.57-(m, 1H), 1.61-1.82(m, 3H), 1.89(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 4.69(m, 1H), 4.77(m, 1H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 6.67(d, J=7.3Hz, 1H), 6.82-7.05(m, 3H), 7.36(m, 1H), 8.11(m, 1H)

Example 60

Preparation of (s)-3-[(s)-2-(2,5-difluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 122 in Table 1)

mp: 102 °C

IR(KBr, cm^{-1}): 3283, 1734, 1637

NMR(CDCl_3 , δ): 0.83(t, J=6.8Hz, 3H), 0.98(d, J=6.0Hz, 3H), 0.99(d, J=5.9Hz, 3H), 1.17-1.37(m, 4H), 1.49-1.82(m, 4H), 1.90(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 4.69(m, 1H), 4.77(m, 1H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 6.64(d, J=6.5Hz, 1H), 7.02-7.23(m, 3H), 7.35(m, 1H), 7.75(m, 1H)

Example 61

Preparation of (s)-3-[(s)-2-(2,6-difluorobenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone

(compd. No. 123 in Table 1)

mp: 116 °C

IR(KBr, cm^{-1}): 3250, 1720, 1670, 1640, 1620

5 NMR(CDCl_3 , δ): 0.87(t, $J=6.7\text{Hz}$, 3H), 0.99(d, $J=5.8\text{Hz}$, 6H), 1.18-1.41(m, 4H), 1.50-1.82(m, 4H), 1.89(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.65-4.86(m, 2H), 6.22(d, $J=3.2\text{Hz}$, 1H), 6.30- (m, 1H), 6.44(d, $J=8.0\text{Hz}$, 1H), 6.73(d, $J=7.6\text{Hz}$, 1H), 6.95(dd, $J=8.1\text{Hz}$, 8.1Hz, 2H), 7.31-7.43(m, 2H)

Example 62

10

Preparation of (s)-3-[(s)-2-(3,4-difluorobenzoylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 124 in Table 1)

mp: 94-100 °C

15 IR(KBr, cm^{-1}): 3315, 1720, 1639, 1602

NMR(CDCl_3 , δ): 0.79(t, $J=7.0\text{Hz}$, 3H), 0.86(d, $J=5.1\text{Hz}$, 6H), 1.09-1.39(m, 4H), 1.47-1.64(m, 1H), 1.64-1.98- (m, 4H), 3.34(s, 2H), 3.73(s, 2H), 4.72(m, 1H), 4.85(m, 1H), 6.22(d, $J=3.2\text{Hz}$, 1H), 6.29(m, 1H), 7.12(ddd, $J=8.6\text{Hz}$, 8.6Hz, 8.6Hz, 1H), 7.35(m, 1H), 7.45-7.63(m, 2H), 7.67(m, 1H), 7.89(m, 1H)

20 Example 63

Preparation of (s)-3-[(s)-2-(3,5-difluorobenzoylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 125 in Table 1)

25 mp: 125-126 °C

IR(KBr, cm^{-1}): 3283, 1723, 1637

NMR(CDCl_3 , δ): 0.84(t, $J=6.7\text{Hz}$, 3H), 0.97(d, $J=6.1\text{Hz}$, 6H), 1.17-1.40(m, 4H), 1.54(m, 1H), 1.64-1.82(m, 3H), 1.90(m, 1H), 3.28(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.68(m, 1H), 4.81(m, 1H), 6.22(d, $J=3.0\text{Hz}$, 1H), 6.31(m, 1H), 6.66(d, $J=7.6\text{Hz}$, 1H), 6.85(d, $J=8.2\text{Hz}$, 1H), 6.95(m, 1H), 7.25-7.31(m, 2H),
30 7.37(m, 1H)

Example 64

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2,3,4-trifluorobenzoylamino)valerylamino]-2-heptanone
35 (compd. No. 126 in Table 1)

mp: 101-102 °C

IR(KBr, cm^{-1}): 3288, 1732, 1660, 1637

NMR(CDCl_3 , δ): 0.83(t, $J=6.8\text{Hz}$, 3H), 0.98(d, $J=6.1\text{Hz}$, 3H), 0.99(d, $J=6.1\text{Hz}$, 3H), 1.17-1.40(m, 4H), 1.47-
40 1.82(m, 4H), 1.91(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.70(m, 1H), 4.80(m, 1H),
6.22(d, $J=3.1\text{Hz}$, 1H), 6.30(m, 1H), 6.61(d, $J=6.0\text{Hz}$, 1H), 6.91(d, $J=9.0\text{Hz}$, 0.5H), 6.95(d, $J=9.0\text{Hz}$, 0.5H),
7.11(m, 1H), 7.36(m, 1H), 7.83(m, 1H)

Example 65

45

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2, 3, 6-trifluorobenzoylamino)valerylamino]-2-heptanone (compd. No. 128 in Table 1)

mp: 116-117 °C

50 IR(KBr, cm^{-1}): 3281, 1734, 1647

NMR(CDCl_3 , δ): 0.88(t, $J=6.8\text{Hz}$, 3H), 0.99(d, $J=4.9\text{Hz}$, 6H), 1.18-1.42(m, 4H), 1.50-1.82(m, 4H), 1.92(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.71(m, 1H), 4.81(m, 1H), 6.22(d, $J=3.2\text{Hz}$, 1H), 6.30(m, 1H), 6.48(d, $J=7.9\text{Hz}$, 1H), 6.64(d, $J=7.3\text{Hz}$, 1H), 6.92(m, 1H), 7.25(m, 1H), 7.36(m, 1H)

55 Example 66

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(3,4,5-trifluorobenzoylamino)valerylamino]-2-heptanone (compd. No. 130 in Table 1)

IR(KBr, cm^{-1}): 3298, 1716, 1639

NMR(CDCl_3 , δ): 0.83(t, $J=6.7\text{Hz}$, 3H), 0.98(d, $J=6.7\text{Hz}$, 6H), 1.13-1.39(m, 4H), 1.47-1.80(m, 4H), 1.91(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.70(m, 1H), 4.78(m, 1H), 6.22(d, $J=2.9\text{Hz}$, 1H), 6.30(m, 1H), 6.92(d, $J=7.6\text{Hz}$, 1H), 7.35(m, 1H), 7.41-7.59(m, 3H)

5

Example 67

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2,3,4,5-tetrafluorobenzoylamino)valeryl amino]-2-heptanone (compd. No. 132 in Table 1)

10

mp: 107-108 °C

IR(KBr, cm^{-1}): 3277, 1705, 1641

NMR(CDCl_3 , δ): 0.84(t, $J=7.0\text{Hz}$, 3H), 0.98(d, $J=5.9\text{Hz}$, 6H), 1.15-1.38(m, 4H), 1.43-1.80(m, 4H), 1.90(m, 1H), 3.27(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.67(m, 1H), 4.81(m, 1H), 6.22(d, $J=3.3\text{Hz}$, 1H), 6.30(m, 1H), 6.57(d, $J=7.6\text{Hz}$, 1H), 6.99(d, $J=8.0\text{Hz}$, 0.5H), 7.03(d, $J=8.0\text{Hz}$, 0.5H), 7.36(m, 1H), 7.70-(m, 1H)

15

Example 68

20 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-pentafluorobenzoylaminovaleryl amino]-2-heptanone (compd. No. 135 in Table 1).

IR(KBr, cm^{-1}): 3287, 1714, 1653

NMR(CDCl_3 , δ): 0.87(t, $J=6.7\text{Hz}$, 3H), 0.98(d, $J=5.4\text{Hz}$, 6H), 1.12-1.39(m, 4H), 1.45-1.79(m, 4H), 1.80-1.98-(m, 1H), 3.31(s, 2H), 3.72(s, 1H), 4.63-4.84(m, 2H), 6.21(d, $J=3.2\text{Hz}$, 1H), 6.30(m, 1H), 6.68(d, $J=7.8\text{Hz}$, 1H), 6.88(d, $J=8.3\text{Hz}$, 1H), 7.35(m, 1H)

25

Example 69

30 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2-toluoylamino)valeryl amino]-2-heptanone (compd. No. 140 in Table 1)

mp: 118-119 °C

IR(KBr, cm^{-1}): 3275, 1734, 1635

35 NMR(CDCl_3 , δ): 0.86(t, $J=6.9\text{Hz}$, 3H), 0.99(d, $J=5.7\text{Hz}$, 6H), 1.17-1.40(m, 4H), 1.44-1.80(m, 4H), 1.91(m, 1H), 2.44(s, 3H), 3.72(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.74(s, 2H), 4.65(m, 1H), 4.80(m, 1H), 6.15(d, $J=8.2\text{Hz}$, 1H), 6.22(d, $J=3.3\text{Hz}$, 1H), 6.30(m, 1H), 6.73(d, $J=8.3\text{Hz}$, 1H), 7.17-7.41(m, 5H)

35

Example 70

40 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(3-toluoylamino)valeryl amino]-2-heptanone (compd. No. 141 in Table 1)

mp: 123-126 °C

45 IR(KBr, cm^{-1}): 3285, 1732, 1635

NMR(CDCl_3 , δ): 0.82(t, $J=6.8\text{Hz}$, 3H), 0.98(d, $J=5.9\text{Hz}$, 6H), 1.15-1.38(m, 4H), 1.56(m, 1H), 1.62-1.99(m, 4H), 2.39(s, 3H), 3.27(d, $J=15\text{Hz}$, 3H), 3.35(d, $J=15\text{Hz}$, 3H), 3.73(s, 2H), 4.65-4.81(m, 2H), 6.22(d, $J=3.0\text{Hz}$, 1H), 6.30(m, 1H), 6.56(d, $J=8.3\text{Hz}$, 1H), 6.77(d, $J=7.7\text{Hz}$, 1H), 7.28-7.34(m, 2H), 7.36(m, 1H), 7.55-7.62(m, 2H)

50

Example 71

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(4-toluoylamino)valeryl amino]-2-heptanone (compd. No. 142 in Table 1)

55

mp: 122-123 °C

IR(KBr, cm^{-1}): 3292, 1732, 1657

NMR(CDCl_3 , δ): 0.81(t, $J=6.7\text{Hz}$, 3H), 0.97(d, $J=5.6\text{Hz}$, 6H), 1.17-1.37(m, 4H), 1.43-1.98(m, 5H), 2.39(s,

3H), 3.27(d, J = 15Hz, 1H), 3.35(d, J = 15Hz, 1H), 3.73(s, 2H), 4.65-4.81(m, 2H), 6.22(d, J = 3.2Hz, 1H), 6.30-(m, 1H), 6.52(d, J = 8.0Hz, 1H), 6.75(d, J = 7.6Hz, 1H), 7.24(d, J = 8.1Hz, 2H), 7.36(m, 1H), 7.67(d, J = 8.1Hz, 2H)

5 Example 72

Preparation of (S)-1-furfurylthio-3-[(S)-4-methyl-2-(2-trifluoromethylbenzoylamino)valerylamino]-2-heptanone (compd. No. 143 in Table 1)

10 mp: 102-106 °C

IR(KBr, cm⁻¹): 3283, 1734, 1641, 1604

NMR(CDCl₃, δ): 0.87(t, J = 6.9Hz, 3H), 0.98(d, J = 5.8Hz, 6H), 1.18-1.39(m, 4H), 1.43-2.0(m, 5H), 3.27(d, J = 15Hz, 1H), 3.35(d, J = 15Hz, 1H), 3.72(s, 2H), 4.62-4.81(m, 2H), 6.21(d, J = 3.2Hz, 1H), 6.29(m, 1H), 6.51-(d, J = 8.4Hz, 1H), 6.89(d, J = 7.6Hz, 1H), 7.35(m, 1H), 7.43-7.62(m, 3H), 7.69(dd, J = 9.0Hz, 2.4Hz, 1H)

15

Example 73

Preparation of (S)-1-furfurylthio-3-[(S)-4-methyl-2-(4-trifluoromethylbenzoylamino)valerylamino]-2-heptanone (compd. No. 145 in Table 1)

20

mp: 121-123 °C

IR(KBr, cm⁻¹): 3289, 1732, 1657, 1639

NMR(CDCl₃, δ): 0.83(t, J = 6.8Hz, 3H), 0.97(d, J = 6.0Hz, 6H), 1.17-1.39(m, 4H), 1.43-1.82(m, 4H), 1.87(m, 1H), 3.28(d, J = 15Hz, 1H), 3.35(d, J = 15Hz, 1H), 3.74(s, 2H), 4.63-4.84(m, 2H), 6.22(d, J = 3.1Hz, 1H), 6.30-(m, 1H), 6.61(d, J = 7.3Hz, 1H), 6.75(d, J = 7.9Hz, 1H), 7.36(m, 1H), 7.69(d, J = 8.4Hz, 2H), 7.89(d, J = 8.4Hz, 2H)

25

Example 74

30 Preparation of (S)-3-[(S)-2-(2-fluoro-6-trifluoromethylbenzoylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 146 in Table 1)

mp: 106-107 °C

IR(KBr, cm⁻¹): 3266, 1720, 1641

35 NMR(CDCl₃, δ): 0.83(t, J = 6.7Hz, 3H), 0.99(d, J = 5.0Hz, 6H), 1.15-1.39(m, 4H), 1.47-2.02(m, 5H), 3.27(d, J = 15Hz, 1H), 3.35(d, J = 15Hz, 1H), 3.73(s, 2H), 4.60-4.80(m, 2H), 6.22(d, J = 3.1Hz, 1H), 6.30(m, 1H), 6.60-(d, J = 7.7Hz, 1H), 7.13(dd, J = 8.0Hz, 7.7Hz, 1H), 7.20-7.36(m, 1H), 7.37(m, 1H), 7.75(m, 1H), 8.38(dd, J = 6.7Hz, 1.9Hz, 1H)

40 Example 75

Preparation of (S)-3-[(S)-2-(2-fluoro-4-trifluoromethylbenzoylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 148 in Table 1)

45 mp: 102-106 °C

IR(KBr, cm⁻¹): 3289, 1732, 1643

NMR(CDCl₃, δ): 0.83(t, J = 6.8Hz, 3H), 0.97(d, J = 6.0Hz, 6H), 1.17-1.39(m, 4H), 1.45-2.0(m, 5H), 3.28(d, J = 15Hz, 1H), 3.36(d, J = 15Hz, 1H), 3.73(s, 2H), 4.63-4.84(m, 2H), 6.22(m, 1H), 6.30(m, 1H), 6.71(d, J = 7.7Hz, 1H), 7.13(dd, J = 11Hz, 8.0Hz, 1H), 7.36(m, 1H), 7.42(d, J = 11Hz, 1H), 7.53(dd, J = 8.0Hz, 0.8Hz, 1H), 8.18(dd, J = 7.9Hz, 7.6Hz, 1H)

50

Example 76

Preparation of (S)-3-[(S)-2-(4-fluoro-3-trifluoromethylbenzoylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone (compd. No. 149 in Table 1)

55

mp: 112-114 °C

IR(KBr, cm⁻¹): 3297, 1715, 1642

EP 0 525 420 A1

NMR(CDCl₃, δ): 0.82(t, J=6.7Hz, 3H), 0.98(d, J=5.2Hz, 6H), 1.15-1.40(m, 4H), 1.45-1.81(m, 4H), 1.87(m, 1H), 3.28(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.74(s, 2H), 4.62-4.83(m, 2H), 6.22(d, J=3.3Hz, 1H), 6.30-(m, 1H), 6.64(d, J=7.1Hz, 1H), 6.93(d, J=6.5Hz, 1H), 7.27(m, 1H), 7.36(m, 1H), 7.99(m, 1H), 8.05(dd, J=6.7Hz, 4.8Hz, 1H)

5

Example 77

Preparation of (s)-1-furfurylthio-3-[(s)-2-(2-methoxybenzoylamino)-4-methylvaleryl-amino]-2-heptanone (compd. No. 151 in Table 1)

10

mp: 77-78 °C

IR(KBr, cm⁻¹): 3306, 2953, 1732, 1660, 1630, 1601

NMR(CDCl₃, δ): 0.77(t, J=6.8Hz, 3H), 0.96(d, J=6.1Hz, 3H), 0.98(d, J=6.1Hz, 3H), 1.17-1.37(m, 4H), 1.45-1.99(m, 5H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.72(s, 2H), 3.97(s, 3H), 4.65-4.78(m, 2H), 6.22(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.95-7.04(m, 2H), 7.09(d, J=7.3Hz, 0.5H), 7.13(d, J=7.3Hz, 0.5H), 7.35(m, 1H), 7.46(d, J=7.3Hz, 0.5H), 7.50(d, J=7.3Hz, 0.5H), 8.17(dd, J=7.8Hz, 1.9Hz, 2H)

15

Example 78

20 Preparation of (s)-1-furfurylthio-3-[(s)-2-(3-methoxyphenoxyacetyl-amino)-4-methylvaleryl-amino]-2-heptanone (compd. No. 103 in Table 1)

IR(neat, cm⁻¹): 3288, 1730, 1651, 1602

NMR(CDCl₃, δ): 0.86(t, J=6.8Hz, 3H), 0.93(d, J=5.9Hz, 6H), 1.17-1.40(m, 4H), 1.47-1.80(m, 4H), 1.83(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 3.79(s, 3H), 4.47(d, J=10Hz, 1H), 4.52(d, J=10Hz, 1H), 4.63(m, 1H), 4.78(m, 1H), 6.22(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.50-6.65(m, 3H), 7.01(t, J=8.7Hz, 2H), 7.20(t, J=8.7Hz, 1H), 7.35(m, 1H)

25

Example 79

30

Preparation of (s)-1-furfurylthio-3-[(s)-2-(4-methoxybenzoylamino)-4-methylvaleryl-amino]-2-heptanone (compd. No. 153 in Table 1)

mp: 124 °C

35 IR(KBr, cm⁻¹): 3291, 1732, 1655, 1624

NMR(CDCl₃, δ): 0.81(t, J=6.1Hz, 3H), 0.98(d, J=5.0Hz, 6H), 1.15-1.35(m, 4H), 1.45-1.95(m, 5H), 3.27(d, J=15Hz, 1H), 3.36(d, J=15Hz, 1H), 3.73(s, 2H), 3.85(s, 3H), 4.63-4.80(m, 2H), 6.23(m, 1H), 6.30(m, 1H), 6.46(d, J=8.7Hz, 1H), 6.75(d, J=7.5Hz, 1H), 6.92(d, J=8.8Hz, 2H), 7.36(m, 1H), 7.75(d, J=8.8Hz, 2H)

Example 80

40 Preparation of (s)-3-[(s)-2-(3,5-dimethoxybenzoylamino)-4-methylvaleryl-amino]-1-furfurylthio -2-heptanone (compd. No. 155 in Table 1)

45 IR(KBr, cm⁻¹): 3279, 1713, 1636

NMR(CDCl₃, δ): 0.82(t, J=6.8Hz, 3H), 0.97(d, J=5.7Hz, 6H), 1.17-1.39(m, 4H), 1.45-1.81(m, 4H), 1.89(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 3.82(s, 6H), 4.62-4.82(m, 2H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 6.55(d, J=6.8Hz, 1H), 6.57(m, 1H), 6.73(d, J=6.9Hz, 1H), 6.89(m, 2H), 7.35(m, 1H)

50

Example 81

Preparation of (s)-1-furfurylthio-3-[(s)-2-(4-methoxycarbonylbenzoylamino)-4-methylvaleryl-amino]-2-heptanone (compd. No. 157 in Table 1)

55

mp: 100-102 °C

IR(KBr, cm⁻¹): 3279, 1726, 1662, 1637

NMR(CDCl₃, δ): 0.82(t, J=6.7Hz, 3H), 0.98(d, J=5.8Hz, 6H), 1.18-1.40(m, 4H), 1.50-1.64(m, 1H), 1.64-2.0(m,

4H), 3.27(d, J=15Hz, 1H), 3.36(d, J=15Hz, 1H), 3.74(s, 2H), 3.95(s, 3H), 4.67-4.83(m, 2H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 6.75(d, J=7.7Hz, 1H), 6.81(d, J=8.3Hz, 1H), 7.36(m, 1H), 7.84(d, J=8.3Hz, 2H), 8.09(d, J=8.3Hz, 2H)

5 Example 82

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(2-naphtoylamino)valeryl-amino]-2-heptanone (compd. No. 162 in Table 1)

mp: 97-99°C

10 IR(KBr, cm⁻¹): 3270, 1700, 1650, 1620

NMR(CDCl₃, δ): 0.77(t, J=6.8Hz, 3H), 1.0(d, J=4.8Hz, 6H), 1.15-2.0(m, 9H), 3.23-3.40(m, 2H), 3.66(s, 0.7H), 3.73(s, 1.3H), 4.70-4.96(m, 2H), 6.21(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.87-7.17(m, 2H), 7.21-7.40(m, 1H), 7.47-7.63(m, 2H), 7.76-8.0(m, 4H), 8.29(s, 1H)

15 Example 83

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(1-naphtoylamino)valeryl-amino]-2-heptanone (compd. No. 161 in Table 1)

20 mp: 81-83°C

IR(KBr, cm⁻¹): 3270, 1720, 1650, 1630

NMR(CDCl₃, δ): 0.87-0.95(m, 3H), 1.01(d, J=6.3Hz, 3H), 1.04(d, J=6.3Hz, 3H), 1.17-2.0(m, 9H), 3.25-3.39(m, 2H), 3.71(s, 0.7H), 3.74(s, 1.3H), 4.75-4.93(m, 2H), 6.19(d, J=3.3Hz, 0.4H), 6.23(d, J=3.3Hz, 0.6H), 6.27-6.31(m, 1H), 6.44(d, J=8Hz, 1H), 6.85(d, J=7Hz, 0.6H), 6.98(d, J=7Hz, 0.4H), 7.30-7.40(m, 1H), 7.41-7.70(m, 4H), 7.92-8.0(m, 2H), 8.27-8.39(m, 1H)

Example 84

Preparation of (s)-1-furfurylthio-3-[(s)-2-(4-methoxycinnamoylamino)-4-methylvaleryl-amino]-2-heptanone (compd. No. 165 in Table 1)

30 IR(KBr, cm⁻¹): 3269, 1715, 1647, 1603

NMR(CDCl₃, δ): 0.81(t, J=6.7Hz, 3H), 0.95(d, J=4.6Hz, 6H), 1.17-1.38(m, 4H), 1.46-1.79(m, 4H), 1.87(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 3.80(s, 3H), 4.67-4.84(m, 2H), 6.21(d, J=3.1Hz, 1H), 6.28(m, 1H), 6.36(d, J=16Hz, 1H), 6.69(d, J=8.4Hz, 1H), 6.83(d, J=8.7Hz, 2H), 7.26(d, J=6.9Hz, 1H), 7.35(m, 1H), 7.41(d, J=8.7Hz, 2H), 7.57(d, J=16Hz, 1H)

Example 85

40 Preparation of (s)-3-[(s)-2-(2,4-dimethoxycinnamoylamino)-3-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 166 in Table 1)

IR(KBr, cm⁻¹): 3270, 1718, 1645, 1604

45 NMR(CDCl₃, δ): 0.86(t, J=8.6Hz, 3H), 0.96(d, J=5.6Hz, 6H), 1.17-1.38(m, 4H), 1.45-1.79(m, 4H), 1.84(m, 1H), 3.27(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 3.83(s, 3H), 3.84(s, 3H), 4.63-4.82(m, 2H), 6.18(d, J=6.8Hz, 1H), 6.22(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.40-6.58(m, 3H), 7.01(d, J=6.4Hz, 1H), 7.31-7.42(m, 2H), 7.79(d, J=16Hz, 1H)

Example 86

50 Preparation of (s)-3-[(s)-2-(1-acetyl-4-piperidylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 168 in Table 1)

mp: 110-112°C

55 IR(KBr, cm⁻¹): 3300, 1715, 1640

NMR(CDCl₃, δ): 0.81-1.01(m, 9H), 1.19-1.39(m, 4H), 1.47-1.78(m, 6H), 1.78-1.97(m, 3H), 2.09(s, 3H), 2.42(m, 1H), 2.67(m, 1H), 3.09(m, 1H), 3.29(d, J=15Hz, 1H), 3.34(d, J=15Hz, 1H), 3.72(s, 2H), 3.86(d, J=13Hz, 1H), 4.45-4.62(m, 2H), 4.68(m, 1H), 6.22(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.71(d, J=6.2Hz, 1H), 7.20(d,

J=7.4Hz, 1H), 7.35(m, 1H)

Example 87

- 5 Preparation of (s)-3-[(s)-2-(1-tert-butoxycarbonyl-4-piperidylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 171 in Table 1)

IR(KBr, cm^{-1}): 3289, 1698, 1640

- 10 NMR(CDCl_3 , δ): 0.78-1.02(m, 9H), 1.13-1.71(m, 10H), 1.45(s, 9H), 1.71-1.97(m, 3H), 2.30(m, 1H), 2.61-2.83-(m, 2H), 3.28(d, J=15Hz, 1H), 3.33(d, J=15Hz, 1H), 3.72(s, 2H), 4.0-4.22(m, 2H), 4.52(m, 1H), 4.69(m, 1H), 6.22(m, 1H), 6.29(m, 1H), 6.43(d, J=8.3Hz, 1H), 7.05(d, J=7.6Hz, 1H), 7.35(m, 1H)

Example 88

- 15 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(4-piperidylcarbonylamino)valeryl-amino]-2-heptanone hydrochloride (compd. No. 172 in Table 1)

IR(KBr, cm^{-1}): 3350, 3250, 1700, 1660, 1635

- 20 NMR(CD_3OD , δ): 0.81-1.05(m, 9H), 1.21-1.43(m, 4H), 1.50-1.78(m, 5H), 1.78-2.17(m, 4H), 2.64(m, 1H), 2.95-3.17(m, 2H), 3.24-3.57(m, 4H), 3.72(s, 2H), 4.39(dd, J=7.0Hz, 7.0Hz, 1H), 4.55(dd, J=9.4Hz, 4.3Hz, 1H), 6.22(d, J=2.7Hz, 1H), 6.32(m, 1H), 7.41(m, 1H)

Example 89

- 25 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-nicotinoylaminovaleryl-amino]-2-heptanone (compd. No. 176 in Table 1)

IR(neat, cm^{-1}): 3280, 1715, 1660, 1630

- 30 NMR(CDCl_3 , δ): 0.80(t, J=7.0Hz, 3H), 0.94(d, J=6.7Hz, 6H), 1.12-1.39(m, 4H), 1.51(m, 1H), 1.67-1.80(m, 3H), 1.84(m, 1H), 3.29(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.73(s, 2H), 4.70-4.84(m, 2H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 6.98(d, J=7.7Hz, 1H), 7.17(d, J=8.0Hz, 1H), 7.30-7.42(m, 2H), 8.11(dd, J=8.0Hz, 1.9Hz, 1H), 8.73(dd, J=4.8Hz, 1.6Hz, 1H), 9.04(d, J=1.9Hz, 1H)

Example 90

- 35 Preparation of (s)-3-[(s)-2-isonicotinoylamino-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 177 in Table 1)

IR(neat, cm^{-1}): 3280, 1715, 1630

- 40 NMR(CDCl_3 , δ): 0.81(t, J=6.7Hz, 3H), 0.92(d, J=4.0Hz, 6H), 1.15-1.39(m, 5H), 1.59(m, 1H), 1.64-1.98(m, 3H), 3.33(s, 2H), 3.73(s, 2H), 4.68-4.95(m, 2H), 6.22(d, J=3.2Hz, 1H), 6.30(m, 1H), 7.35(d, J=1.9Hz, 1H), 7.43(d, J=6.7Hz, 1H), 7.58-7.71(m, 2H), 7.81(d, J=7.5Hz, 1H), 8.65-8.69(m, 2H)

Example 91

- 45 Preparation of (s)-3-[(s)-2-(2-benzofuranylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 180 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1640

- 50 NMR(CDCl_3 , δ): 0.81(t, J=6.9Hz, 2.2H), 0.89(t, J=6.9Hz, 0.8H), 1.0(d, J=6.5Hz, 6H), 1.10-1.99(m, 9H), 3.23-3.40(m, 2H), 3.70(d, J=5.4Hz, 0.5H), 3.73(s, 1.5H), 4.76-4.93(m, 2H), 6.18(m, 1H), 6.30(m, 1H), 6.70-(d, J=7Hz, 0.75H), 6.76(d, J=7Hz, 0.25H), 7.05(d, J=8Hz, 1H), 7.25-7.59(m, 5H), 7.67(d, J=7.4Hz, 1H)

Example 92

- 55 Preparation of (s)-3-[(s)-2-(3-benzofuranylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-2-heptanone (compd. No. 181 in Table 1)

mp: 113-116 °C

IR(KBr, cm⁻¹): 3300, 1710, 1630

NMR(CDCl₃, δ): 0.77(t, J=6.7Hz, 3H), 0.83-1.02(m, 6H), 1.07-1.38(m, 5H), 1.41-1.63(m, 1H), 1.63-1.97(m, 3H), 3.30(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.72(s, 2H), 4.70(m, 1H), 4.80(dt, J=7.1Hz, 7.0Hz, 1H),
 5 6.21(d, J=3.1Hz, 1H), 6.28(m, 1H), 7.21-7.38(m, 4H), 7.38-7.57(m, 2H), 7.93(m, 1H), 8.23(d, J=1.4Hz, 1H)

Example 93

Preparation of (s)-3-[(s)-2-(7-fluoro-2-benzofuranylcarbonylamino)-4-methylvalerylamino]-1-furfuryl thio-2-heptanone (compd. No. 182 in Table 1)

mp: 102-103 °C

IR(KBr, cm⁻¹): 3270, 1700, 1650

NMR(CDCl₃, δ): 0.79(t, J=6.8Hz, 3H), 0.98(d, J=4.9Hz, 6H), 1.18-1.40(m, 4H), 1.60(m, 1H), 1.64-1.97(m, 4H), 3.32(d, J=15Hz, 1H), 3.40(d, J=15Hz, 1H), 3.75(s, 2H), 4.75-4.95(m, 2H), 6.23(d, J=3.1Hz, 1H), 6.29-
 15 (m, 1H), 7.08-7.35(m, 5H), 7.37(s, 1H), 7.42(dd, J=7.5Hz, 1.1Hz, 1H)

Example 94

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(4-oxo-4H-1-benzopyran-4-ylcarbonylamino)valerylamino]-2-heptanone (compd. No. 188 in Table 1)

mp: 114-115 °C

IR(KBr, cm⁻¹): 3350, 3250, 1705, 1660, 1625

NMR(CDCl₃, δ): 0.84(t, J=6.8Hz, 3H), 1.0(d, J=9.2Hz, 6H), 1.15-2.0(m, 9H), 3.30(d, J=15Hz, 1H), 3.38(d, J=15Hz, 1H), 3.75(s, 2H), 4.69(m, 1H), 4.82(m, 1H), 6.23(d, J=2.9Hz, 1H), 6.31(m, 1H), 6.61(d, J=8Hz, 1H), 7.16(s, 1H), 7.36-7.55(m, 3H), 7.57(d, J=14Hz, 1H), 7.72-7.80(m, 1H), 8.22(dd, J=1.6Hz, 7.9Hz, 1H)

Example 95

Preparation of (s)-3-[(2s, 3s)-2-benzyloxycarbonylamino-3-methylvalerylamino]-1-furfurylthio -2-heptanone (compd. No. 205 in Table 1)

mp: 101-103 °C

IR(KBr, cm⁻¹): 3300, 3250, 1705, 1680, 1640

NMR(CDCl₃, δ): 0.83-1.10(m, 9H), 1.07-1.39(m, 3H), 1.42-1.78(m, 4H), 1.82-2.01(m, 2H), 3.26(d, J=15Hz, 1H), 3.34(d, J=15Hz, 1H), 3.71(s, 2H), 4.05(dt, J=8.0Hz, 6.4Hz, 1H), 4.80(m, 1H), 5.12(s, 2H), 5.30(d, J=7.7Hz, 1H), 6.22(d, J=3.3Hz, 1H), 6.30(m, 1H), 6.43(d, J=8.0Hz, 1H), 7.30-7.41(m, 6H)

Example 96

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-hexanoylamino]-1-furfurylthio-2-heptanone (compd. No. 206 in Table 1)

mp: 95-97 °C

IR(KBr, cm⁻¹): 3280, 1730, 1690, 1650

NMR(CDCl₃, δ): 0.82-0.99(m, 6H), 1.12-1.45(m, 8H), 1.49-1.65(m, 2H), 1.75-1.99(m, 2H), 3.27(d, J=15Hz, 1H), 3.34(d, J=15Hz, 1H), 3.71(s, 2H), 4.16(td, J=7.3Hz, 6.4Hz, 1H), 4.76(m, 1H), 5.12(s, 2H), 5.26(d, J=7.9Hz, 1H), 6.21(d, J=3.1Hz, 1H), 6.29(m, 1H), 6.56(d, J=6.4Hz, 1H), 7.29-7.39(m, 6H)

Example 97

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-3-phenylpropionylamino]-1-furfurylthio-2-heptanone (compd. No. 208 in Table 1)

mp: 123-124 °C

IR(KBr, cm⁻¹): 3300, 1720, 1710, 1680, 1640

NMR(CDCl₃, δ): 0.85(t, J=6.9Hz, 3H), 1.0-1.38(m, 2H), 1.51(m, 1H), 1.61-1.69(m, 2H), 1.83(m, 1H), 3.03(dd, J=14Hz, 7.0Hz, 1H), 3.15(dd, J=14Hz, 7.0Hz, 1H), 3.15(d, J=15Hz, 1H), 3.22(d, J=15Hz, 1H), 3.67(s, 2H),

4.45(td, J=6.9Hz, 6.9Hz, 1H), 4.70(m, 1H), 5.09(s, 2H), 5.27(d, J=5.6Hz, 1H), 6.21(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.40(d, J=6.9Hz, 1H), 7.09-7.21(m, 2H), 7.21-7.42(m, 9H)

Example 98

5

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-3-tert-butoxypropionylamino)-1-furfurylthio-2-heptanone (compd. No. 210 in Table 1)

mp: 71-73 °C

10

IR(KBr, cm⁻¹): 3300, 1720, 1690, 1660, 1640

NMR(CDCl₃, δ): 0.88(t, J=6.8Hz, 3H), 1.16(s, 9H), 1.24-1.41(m, 4H), 1.59(m, 1H), 1.91(m, 1H), 3.24(d, J=15Hz, 1H), 3.30(d, J=15Hz, 1H), 3.42(dd, J=7.2Hz, 7.2Hz, 1H), 3.71(s, 2H), 3.84(m, 1H), 4.26(m, 1H), 4.77(m, 1H), 5.10(d, J=12Hz, 1H), 5.16(d, J=12Hz, 1H), 5.71(d, J=5.1Hz, 1H), 6.21(d, J=3.2Hz, 1H), 6.29(m, 1H), 7.23(d, J=5.1Hz, 1H), 7.35-7.41(m, 6H)

15

Example 99

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-tert-butoxycarbonylpropionylamino)-1-furfurylthio-2-heptanone (compd. No. 213 in Table 1)

20

mp: 77-78 °C

IR(KBr, cm⁻¹): 3300, 1720, 1690, 1650

NMR(CDCl₃, δ): 0.88(t, J=6.8Hz, 3H), 1.18-1.38(m, 4H), 1.43(s, 9H), 1.58(m, 1H), 1.84(m, 1H), 2.62(dd, J=17Hz, 6.5Hz, 1H), 2.96(dd, J=17Hz, 4.1Hz, 1H), 3.24(d, J=15Hz, 1H), 3.32(d, J=15Hz, 1H), 3.71(s, 2H), 4.54(m, 1H), 4.72(m, 1H), 5.15(s, 2H), 5.98(d, J=8.5Hz, 1H), 6.22(d, J=2.3Hz, 1H), 6.30(m, 1H), 7.10(d, J=7.0Hz, 1H), 7.30-7.43(m, 6H)

25

Example 100

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-tert-butoxycarbonylbutyrylamino)-1-furfurylthio-2-heptanone (compd. No. 216 in Table 1)

30

mp: 78-79 °C

IR(KBr, cm⁻¹): 3300, 1730, 1710, 1690, 1650

35

NMR(CDCl₃, δ): 0.88(t, J=6.8Hz, 3H), 1.18-1.39(m, 4H), 1.44(s, 9H), 1.50-1.70(m, 1H), 1.81-2.17(m, 3H), 2.31-2.49(m, 2H), 3.26(d, J=15Hz, 1H), 3.29(d, J=15Hz, 1H), 3.72(s, 2H), 4.25(dt, J=7.4Hz, 6.8Hz, 1H), 4.75(m, 1H), 5.11(s, 2H), 5.73(d, J=6.8Hz, 1H), 6.22(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.82(d, J=7.4Hz, 1H), 7.27-7.39(m, 6H)

Example 101

40

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-carboxybutyrylamino)-1-furfurylthio-2-heptanone (compd. No. 217 in Table 1)

mp: 67-71 °C

IR(KBr, cm⁻¹): 3300, 1720, 1705, 1680, 1650

45

NMR(CDCl₃, δ): 0.81-0.98(m, 3H), 1.18-1.43(m, 4H), 1.60(m, 1H), 1.72-2.0(m, 2H), 2.10(m, 1H), 2.37(t, J=7.5Hz, 2H), 3.23-3.37(m, 2H), 3.72(s, 2H), 4.15(dt, J=5.0Hz, 3.9Hz, 1H), 4.57(m, 1H), 5.08(s, 2H), 6.22(d, J=2.9Hz, 1H), 6.31(m, 1H), 7.21-7.39(m, 5H), 7.40(m, 1H)

Example 102

50

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-6-tert-butoxycarbonylamino)hexanoylamino)-1-furfurylthio-2-heptanone (compd. No. 220 in Table 1)

mp: 60-63 °C

55

IR(KBr, cm⁻¹): 3350, 1725, 1690, 1650

NMR(CDCl₃, δ): 0.87(t, J=6.7Hz, 3H), 1.15-1.78(m, 10H), 1.41(s, 9H), 1.79-1.99(m, 2H), 2.97-3.18(m, 2H), 3.25(d, J=15Hz, 1H), 3.35(d, J=15Hz, 1H), 3.71(s, 2H), 4.18(m, 1H), 4.59-4.82(m, 2H), 5.10(s, 2H), 5.63(m, 1H), 6.22(d, J=2.9Hz, 1H), 6.29(m, 1H), 6.78(d, J=7.8Hz, 1H), 7.24-7.41(m, 6H)

Example 103

Preparation of (s)-3-((s)-6-amino-2-benzyloxycarbonylaminoheptanoylamino)-1-furfurylthio-2-hept anone hydrochloride (compd. No. 221 in Table 1)

5

mp: 95° C(dec.)

IR(KBr, cm⁻¹): 3310, 1720, 1680, 1635

NMR(CDCl₃, δ): 0.85-1.05(m, 3H), 1.22-1.42(m, 4H), 1.42-2.0(m, 8H), 2.96(t, J = 7.5Hz, 2H), 3.44(s, 2H), 3.76-
 10 7.43(m, 5H), 7.46(m, 1H), 8.33(d, J = 7.9Hz, 1H)

Example 104

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-2-phenylacetyl-amino)-1-furfurylthio-2-heptanone (compd. No. 224 in Table 1)

15

mp: 144-146° C

IR(KBr, cm⁻¹): 3300, 1710, 1640

NMR(CDCl₃, δ): 0.87(t, J = 7.1Hz, 3H), 1.07-1.39(m, 4H), 1.42-1.63(m, 1H), 1.81-1.99(m, 1H), 3.13(s, 2H),
 20 3.54(d, J = 15Hz, 1H), 3.59(d, J = 15Hz, 1H), 4.71(m, 1H), 5.03(d, J = 12Hz, 1H), 5.11(d, J = 12Hz, 1H), 5.23(d, J = 6.1Hz, 1H), 6.07(d, J = 6.3Hz, 1H), 6.10(d, J = 3.1Hz, 1H), 6.21(m, 1H), 6.31(d, J = 7.4Hz, 1H), 7.24-7.43-
 (m, 11H)

Example 105

25

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(2-pyridylmethylthio)-2-heptanone (compd. No. 226 in Table 1)

IR(neat, cm⁻¹): 3304, 1711, 1658

30 NMR(CD₃OD, δ): 0.80-1.0(m, 9H), 1.16-1.40(m, 4H), 1.45-1.98(m, 5H), 3.25-3.40(m, 2H), 3.80(s, 2H), 4.15(m, 1H), 4.57(m, 1H), 5.07(s, 2H), 7.25-7.39(m, 6H), 7.42(d, J = 7.8Hz, 1H), 7.76(ddd, J = 7.7Hz, 7.7Hz, 1.8Hz, 1H), 8.44(m, 1H)

Example 106

35

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(3-pyridylmethylthio)-2-heptanone (compd. No. 228 in Table 1)

IR(neat, cm⁻¹): 3409, 1717, 1653

40 NMR(CD₃OD, δ): 0.92-1.03(m, 9H), 1.18-1.43(m, 4H), 1.47-1.98(m, 5H), 3.36(d, J = 15Hz, 1H), 3.42(d, J = 15Hz, 1H), 3.94(s, 2H), 4.15(dd, J = 7.6Hz, 7.5Hz, 1H), 4.48(dd, J = 9.6Hz, 4.4Hz, 1H), 5.06(d, J = 10Hz, 1H), 5.11(d, J = 10Hz, 1H), 7.21-7.40(m, 5H), 8.04(dd, J = 8.0Hz, 5.8Hz, 1H), 8.62(d, J = 8.0Hz, 1H), 8.75(d, J = 5.8Hz, 1H), 8.83(s, 1H)

Example 107

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(4-pyridylmethylthio)-2-heptanone (compd. No. 230 in Table 1)

50

IR(neat, cm⁻¹): 3300, 1720, 1705, 1660, 1600

NMR(CDCl₃, δ): 0.86(t, J = 6.7Hz, 3H), 0.91-0.95(m, 6H), 1.13-1.39(m, 5H), 1.41-1.78(m, 3H), 1.84(m, 1H), 3.11(d, J = 15Hz, 1H), 3.24(d, J = 15Hz, 1H), 3.63(s, 2H), 4.22(m, 1H), 4.75(m, 1H), 5.11(s, 2H), 5.38(d, J = 8.0Hz, 1H), 6.81(d, J = 6.9Hz, 1H), 7.15-7.31(m, 2H), 7.31-7.41(m, 5H), 8.45-8.60(m, 2H)

Example 108

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-cyclohexyl -1-methylthio-2-butanone (compd. No. 236 in Table 1)

mp: 83-84 °C

IR(KBr, cm^{-1}): 3320, 1684, 1648

NMR(CDCl_3 , δ): 0.90-1.05(m, 8H), 1.05-1.88(m, 14H), 2.06(s, 3H), 3.20(d, $J=14\text{Hz}$, 1H), 3.38(d, $J=14\text{Hz}$, 1H), 4.18(m, 1H), 4.88(m, 1H), 5.12(s, 2H), 5.13(m, 1H), 6.43(d, $J=7\text{Hz}$, 1H), 7.35(s, 5H)

5

Example 109

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-cyclohexyl -1-furfurylthio-2-butanone (compd. No. 238 in Table 1)

10

IR(neat, cm^{-1}): 3320, 1700, 1650

NMR(CDCl_3 , δ): 0.78-1.0(m, 8H), 1.04-1.85(m, 14H), 3.24(d, $J=13\text{Hz}$, 1H), 3.35(d, $J=13\text{Hz}$, 1H), 3.71(s, 2H), 4.10(m, 1H), 4.78(m, 1H), 5.07(m, 1H), 5.12(s, 2H), 6.22(d, $J=3.2\text{Hz}$, 1H), 6.30(m, 1H), 6.38(d, $J=8\text{Hz}$, 1H), 7.35(s, 5H), 7.39(m, 1H)

15

Example 110

Preparation of (s)-4-cyclohexyl-1-furfurylthio-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-2-butanone (compd. No. 240 in Table 1)

20

IR(neat, cm^{-1}): 3310, 1710, 1650

NMR(CDCl_3 , δ): 0.88-1.07(m, 8H), 1.07-1.88(m, 14H), 3.28(d, $J=15\text{Hz}$, 1H), 3.36(d, $J=15\text{Hz}$, 1H), 3.73(s, 2H), 4.53(s, 2H), 4.57(m, 1H), 4.80(m, 1H), 6.21(d, $J=3.2\text{Hz}$, 1H), 6.32(m, 1H), 6.48(d, $J=8\text{Hz}$, 1H), 6.87-6.99(m, 3H), 7.05(t, $J=8\text{Hz}$, 1H), 7.30-7.40(m, 3H)

25

Example 111

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-mercapto -4-phenyl-2-butanone (compd. No. 242 in Table 1)

30

mp: 171 °C

IR(KBr, cm^{-1}): 3320, 1720, 1690, 1655

NMR(CDCl_3 , δ): 0.80-1.0(m, 6H), 1.30-1.70(m, 3H), 2.92(dd, $J=7.6\text{Hz}$, 14Hz, 1H), 3.03-3.25(m, 2H), 3.38(d, $J=15\text{Hz}$, 1H), 4.13(m, 1H), 4.85(m, 1H), 4.95-5.18(m, 2H), 5.25(m, 1H), 6.76(d, $J=7\text{Hz}$, 1H), 7.05-7.45(m, 10H)

35

Example 112

Preparation of (s)-3-((s)-2-tert-butoxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -4-phenyl-2-butanone (compd. No. 243 in Table 1)

40

mp: 117-118 °C

IR(KBr, cm^{-1}): 3360, 1705, 1660

NMR(CDCl_3 , δ): 0.85-1.05(m, 6H), 1.25-1.70(m, 3H), 1.44(s, 9H), 1.98(s, 3H), 2.95-3.25(m, 4H), 4.04(m, 1H), 4.77(m, 1H), 5.06(m, 1H), 6.67(m, 1H), 7.15-7.38(m, 5H)

45

Example 113

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -4-phenyl-2-butanone (compd. No. 244 in Table 1)

50

mp: 81-91 °C

IR(KBr, cm^{-1}): 3340, 3290, 1720, 1683, 1652

NMR(CDCl_3 , δ): 0.89(d, $J=5.8\text{Hz}$, 6H), 1.30-1.65(m, 3H), 1.99(s, 3H), 2.90-3.25(m, 4H), 4.10(m, 1H), 4.95-5.15(m, 2H), 5.10(s, 2H), 6.55(m, 1H), 7.08-7.43(m, 10H)

55

Example 114

Preparation of (s)-3-[(s)-N-methyl-2-(benzyloxycarbonylamino)-4-methylvaleryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 245 in Table 1)

IR(neat, cm^{-1}): 3300, 1720, 1640

5 NMR(CDCl_3 , δ): 0.85-1.0(m, 6H), 1.20-1.82(m, 3H), 2.0(s, 3H), 2.84(s, 3H), 2.97(d, J = 14Hz, 1H), 3.0(d, J = 14Hz, 1H), 3.26(d, J = 14Hz, 1H), 3.35(d, J = 14Hz, 1H), 4.54(m, 1H), 4.90(m, 1H), 5.07(s, 2H), 5.26(d, J = 8Hz, 1H), 7.15-7.35(m, 10H)

Example 115

10

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-methylsulfinyl-4-phenyl-2-butanone (compd. No. 248 in Table 1)

mp: 97-102 °C

15 IR(KBr, cm^{-1}): 3320, 1715, 1685, 1648

NMR(CDCl_3 , δ): 0.70-0.95(m, 6H), 1.10-1.70(m, 3H), 2.84(s, 2.1H), 2.87(s, 0.9H), 2.80-3.03(m, 3H), 3.13-3.45(m, 2H), 3.50-3.75(m, 1H), 4.0-4.20(m, 1H), 4.28-4.88(m, 2H), 4.95-5.10(m, 1H), 5.09(s, 1.4H), 5.13(s, 0.6H), 7.10-7.55(m, 10H)

20 Example 116

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-methylsulfonyl-4-phenyl-2-butanone (compd. No. 249 in Table 1)

25 mp: 142-144 °C

IR(KBr, cm^{-1}): 3400, 3200, 1718, 1652

NMR($\text{DMSO}-d_6$, δ): 0.78(d, J = 8.4Hz, 3H), 0.82(d, J = 8.4Hz, 3H), 1.15-1.65(m, 3H), 2.78(m, 1H), 3.06(s, 3H), 3.18(m, 1H), 3.34(s, 2H), 3.95(m, 1H), 4.40-4.60(m, 2H), 5.01(s, 2H), 7.13-7.58(m, 10H), 8.50(d, J = 8Hz, 1H)

30 Example 117

Preparation of (s)-3-[(s)-2-amino-4-methylvaleryl-amino]-1-methylthio-4-phenyl-2-butanone hydrochloride (compd. No. 250 in Table 1)

35 mp: 141 °C

IR(KBr, cm^{-1}): 3400, 1698, 1658

NMR($\text{DMSO}-d_6$, δ): 0.85(d, J = 2.4Hz, 3H), 0.87(d, J = 2.3Hz, 3H), 1.45-1.70(m, 3H), 1.97(s, 3H), 2.88(dd, J = 8.8Hz, 14Hz, 1H), 3.16(dd, J = 5.1Hz, 14Hz, 1H), 3.43(d, J = 15Hz, 1H), 3.53(d, J = 15Hz, 1H), 3.75(m, 1H), 4.77(m, 1H), 7.15-7.35(m, 5H), 8.28(s, 3H), 9.11(d, J = 7.3Hz, 1H)

40

Example 118

Preparation of (s)-3-[(s)-2-acetyl-amino-4-methylvaleryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 251 in Table 1)

45

mp: 118-120 °C

IR(KBr, cm^{-1}): 3320, 1720, 1645

NMR(CDCl_3 , δ): 0.89(d, J = 4.0Hz, 3H), 0.91(d, J = 4.1Hz, 3H), 1.35-1.70(m, 3H), 1.95(s, 3H), 1.99(s, 3H), 2.90-3.25(m, 4H), 4.40(m, 1H), 5.06(q, J = 6.8Hz, 1H), 5.83(d, J = 7Hz, 1H), 6.77(d, J = 7Hz, 1H), 7.15-7.38(m, 5H)

50

Example 119

Preparation of (s)-3-[(s)-4-methyl-2-(3-phenylpropionyl-amino)valeryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 254 in Table 1)

55

mp: 104-107 °C

IR(KBr, cm^{-1}): 3320, 3275, 1715, 1640

NMR(CDCl₃, δ): 0.83(d, J=3.8Hz, 3H), 0.85(d, J=3.9Hz, 3H), 1.25-1.65(m, 3H), 1.99(s, 3H), 2.40-2.58(m, 2H), 2.85-3.22(m, 6H), 4.37(m, 1H), 5.07(q, J=7.2Hz, 1H), 5.61(d, J=7.6Hz, 1H), 6.64(d, J=7.6Hz, 1H), 7.10-7.35(m, 10H)

5 Example 120

Preparation of (s)-3-[(s)-4-methyl-2-(1-naphtylacetyl-amino)valeryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 256 in Table 1)

10 mp: 126-129 °C

IR(KBr, cm⁻¹): 3300, 1720, 1650

NMR(CDCl₃, δ): 0.55-0.68(m, 6H), 0.98-1.45(m, 3H), 1.99(s, 3H), 2.84(m, 1H), 3.0-3.20(m, 3H), 3.90-4.10(m, 2H), 4.30(m, 1H), 4.94(m, 1H), 5.38(d, J=8Hz, 0.7H), 5.50(d, J=8Hz, 0.3H), 6.53(m, 1H), 7.03-7.54(m, 9H), 7.78-7.92(m, 3H)

15

Example 121

Preparation of (s)-3-[(s)-4-methyl-2-(2-naphtylacetyl-amino)valeryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 257 in Table 1)

20

mp: 112-114 °C

IR(KBr, cm⁻¹): 3300, 1730, 1645

NMR(CDCl₃, δ): 0.73-0.83(m, 6H), 1.20-1.60(m, 3H), 1.97(s, 0.9H), 1.98(s, 2.1H), 2.96(m, 1H), 3.04-3.20(m, 3H), 3.62-3.75(m, 2H), 4.37(m, 1H), 5.01(q, J=6.7Hz, 1H), 5.62(d, J=8Hz, 0.7H), 5.70(d, J=8Hz, 0.3H), 6.61(m, 1H), 7.05-7.19(m, 2H), 7.22-7.35(m, 4H), 7.40-7.56(m, 2H), 7.63-7.72(m, 1H), 7.75-7.90(m, 3H)

25

Example 122

Preparation of (s)-3-[(s)-4-methyl-2-phenylsulfonylaminovaleryl-amino]-1-methylthio-4-phenyl-2-butanone (compd. No. 262 in Table 1)

30

mp: 133-136 °C

IR(KBr, cm⁻¹): 3350, 3280, 1700, 1675, 1645

NMR(CDCl₃, δ): 0.50-0.90(m, 6H), 1.20-1.60(m, 3H), 1.97(s, 1.8H), 1.98(s, 1.2H), 2.80-3.20(m, 4H), 3.63(m, 1H), 4.90-5.10(m, 2H), 6.41(d, J=7Hz, 0.4H), 6.62(d, J=7Hz, 0.6H), 7.09-7.35(m, 5H), 7.45-7.64(m, 3H), 7.73-7.95(m, 2H)

35

Example 123

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-octylthio-4-phenyl-2-butanone (compd. No. 268 in Table 1)

40

mp: 69 °C

IR(KBr, cm⁻¹): 3340, 3305, 1715, 1690, 1650

NMR(CDCl₃, δ): 0.75-1.0(m, 9H), 1.15-1.70(m, 15H), 2.35(t, J=7.2Hz, 2H), 2.90-3.25(m, 4H), 4.0-4.20(m, 1H), 4.88-5.20(m, 2H), 5.08(s, 2H), 6.56(m, 1H), 7.07-7.45(m, 10H)

45

Example 124

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-(2-chloroethylthio)-4-phenyl-2-butanone (compd. No. 271 in Table 1)

50

mp: 77-80 °C

IR(KBr, cm⁻¹): 3310, 3270, 1715, 1680, 1650

NMR(CDCl₃, δ): 0.83-1.0(m, 6H), 1.38-1.60(m, 3H), 2.65-2.85(m, 2H), 3.0-3.30(m, 4H), 3.45-3.65(m, 2H), 4.11(m, 1H), 4.90-5.08(m, 2H), 5.10(s, 2H), 6.65(m, 1H), 7.10-7.35(m, 10H)

55

Example 125

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(2-methoxyethylthio)-4-phenyl-2-butanone (compd. No. 272 in Table 1)

mp: 68-69 °C

5 IR(KBr, cm^{-1}): 3340, 3300, 1725, 1685, 1660

NMR(CDCl_3 , δ): 0.90(d, $J=5.9\text{Hz}$, 6H), 1.30-1.75(m, 3H), 2.61(t, $J=6.2\text{Hz}$, 2H), 3.0(dd, $J=6.8\text{Hz}$, 13Hz, 1H), 3.16(dd, $J=6.8\text{Hz}$, 13Hz, 1H), 3.26(d, $J=4.5\text{Hz}$, 2H), 3.32(s, 3H), 3.50(t, $J=6.2\text{Hz}$, 2H), 4.12(m, 1H), 4.97(m, 1H), 5.07(d, $J=7\text{Hz}$, 1H), 5.10(s, 2H), 6.59(d, $J=7\text{Hz}$, 1H), 7.10-7.35(m, 10H)

10 Example 126

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(2-dimethylaminoethylthio)-4-phenyl-2-butanone (compd. No. 275 in Table 1)

15 mp: 67-69 °C

IR(KBr, cm^{-1}): 3320, 1710, 1655

NMR(CDCl_3 , δ): 0.90-1.0(m, 6H), 1.20-1.75(m, 3H), 2.28(s, 3H), 2.31(s, 3H), 2.50-2.75(m, 4H), 2.98(m, 1H), 3.08-3.32(m, 2H), 3.44(m, 1H), 4.18(m, 1H), 4.97-5.35(m, 2H), 5.10(s, 2H), 6.85(m, 1H), 7.13-7.50(m, 10H)

20 Example 127

Preparation of (s)-1-(2-acetylaminoethylthio) -3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino) -4-phenyl-2-butanone (compd. No. 276 in Table 1)

25 mp: 122-123 °C

IR(KBr, cm^{-1}): 3320, 1725, 1690, 1642

NMR(CDCl_3 , δ): 0.83-0.98(m, 6H), 1.30-1.70(m, 3H), 1.97(s, 3H), 2.45-2.68(m, 2H), 2.90-3.45(m, 6H), 4.12(m, 1H), 4.95-5.15(m, 2H), 5.09(s, 2H), 6.21(m, 1H), 6.68(d, $J=7\text{Hz}$, 1H), 7.10-7.40(m, 10H)

30 Example 128

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-benzylthio -4-phenyl-2-butanone (compd. No. 277 in Table 1)

35 mp: 86-87 °C

IR(KBr, cm^{-1}): 3320, 1700, 1680, 1658

NMR(CDCl_3 , δ): 0.87(d, $J=6.0\text{Hz}$, 3H), 0.89(d, $J=6.1\text{Hz}$, 3H), 1.35-1.70(m, 3H), 2.88-3.22(m, 4H), 3.69(s, 2H), 4.12(m, 1H), 4.95-5.18(m, 2H), 5.09(s, 2H), 6.53(m, 1H), 7.10-7.50(m, 15H)

40 Example 129

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-phenyl-1- phenylthio-2-butanone (compd. No. 279 in Table 1)

45 mp: 105-106 °C

IR(KBr, cm^{-1}): 3330, 3280, 1713, 1685, 1653

NMR(CDCl_3 , δ): 0.87(d, $J=6.2\text{Hz}$, 6H), 1.30-1.70(m, 3H), 2.88-3.18(m, 2H), 3.63(s, 2H), 4.13(m, 1H), 4.95-5.18(m, 2H), 5.09(s, 2H), 6.53(m, 1H), 7.05-7.15(m, 2H), 7.15-7.50(m, 13H)

50 Example 130

Preparation of (s)-3-benzyloxycarbonylaminoacetyl-amino-1-furfurylthio -4-phenyl-2-butanone (compd. No. 280 in Table 1)

55 IR(neat, cm^{-1}): 3320, 1720, 1670

MR(CDCl_3 , δ): 2.95-3.20(m, 2H), 3.16(s, 2H), 3.63(s, 2H), 3.83(d, $J=5.7\text{Hz}$, 2H), 5.06(q, $J=6.8\text{Hz}$, 1H), 5.12-(s, 2H), 5.30(m, 1H), 6.18(m, 1H), 6.29(m, 1H), 6.53(d, $J=7\text{Hz}$, 1H), 7.07-7.50(m, 11H)

Example 131

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-3-methylbutyrylamino)-1-furfurylthio -4-phenyl-2-butanone (compd. No. 282 in Table 1)

mp: 122-125 °C

IR(KBr, cm^{-1}): 3340, 3290, 1732, 1692, 1661

NMR(CDCl_3 , δ): 0.81(d, J=6.8Hz, 3H), 0.90(d, J=6.7Hz, 3H), 2.07(m, 1H), 2.92-3.25(m, 4H), 3.62(s, 2H), 3.96(m, 1H), 4.98-5.28(m, 2H), 5.11(s, 2H), 6.18(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.44(d, J=8Hz, 1H), 7.08-7.50(m, 11H)

Example 132

Preparation of (s)-1-furfurylthio-3-((s)-2-isobutoxycarbonylamino-4-methylvaleryl-amino)-4-phenyl-2-butanone (compd. No. 284 in Table 1)

mp: 89-90 °C

IR(KBr, cm^{-1}): 3340, 3290, 1730, 1690, 1655

NMR(CDCl_3 , δ): 0.83-0.98(m, 12H), 1.30-1.70(m, 3H), 1.92(m, 1H), 2.98(dd, J=7.5Hz, 14Hz, 1H), 3.08-3.25(m, 3H), 3.63(s, 2H), 3.83(d, J=6.6Hz, 2H), 4.13(m, 1H), 4.88(m, 1H), 5.02(d, J=7.5Hz, 1H), 6.19(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.57(d, J=7Hz, 1H), 7.15(d, J=7.7Hz, 2H), 7.19-7.32(m, 3H), 7.35(m, 1H)

Example 133

Preparation of (s)-3-((s)-2-tert-butoxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio -4-phenyl-2-butanone (compd. No. 285 in Table 1)

IR(KBr, cm^{-1}): 3320, 1705, 1690, 1655

NMR(CDCl_3 , δ): 0.89(d, J=6.1Hz, 3H), 0.91(d, J=6.2Hz, 3H), 1.30-1.75(m, 3H), 1.43(s, 9H), 3.01(dd, J=7.0Hz, 14Hz, 1H), 3.14(dd, J=6.8Hz, 14Hz, 1H), 3.16(s, 2H), 3.62(s, 2H), 4.08(m, 1H), 4.75(m, 1H), 5.02(m, 1H), 6.18(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.65(d, J=7Hz, 1H), 7.10-7.20(m, 2H), 7.20-7.32(m, 3H), 7.35(m, 1H)

Example 134

Preparation of (s)-3-((s)-2-cyclopentylmethoxycarbonylamino-3-methylvaleryl-amino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 287 in Table 1)

mp: 77-78 °C

IR(KBr, cm^{-1}): 3340, 3290, 1715, 1692, 1660

NMR(CDCl_3 , δ): 0.89(d, J=6.0Hz, 3H), 0.91(d, J=6.1Hz, 3H), 1.15-1.83(m, 11H), 2.16(m, 1H), 3.01(dd, J=6.5Hz, 14Hz, 1H), 3.07-3.25(m, 3H), 3.63(s, 2H), 3.93(d, J=7.1Hz, 2H), 4.13(m, 1H), 4.87(m, 1H), 5.0(q, J=7.3Hz, 1H), 6.18(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.62(d, J=7Hz, 1H), 7.14(d, J=6.1Hz, 2H), 7.16-7.35(m, 4H)

Example 135

Preparation of (s)-3-((s)-2-cyclohexylmethoxycarbonylamino-3-methylvaleryl-amino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 288 in Table 1)

IR(neat, cm^{-1}): 3330, 1735, 1692, 1660

NMR(CDCl_3 , δ): 0.80-1.05(m, 8H), 1.10-1.80(m, 12H), 3.01(dd, J=6.8Hz, 14Hz, 1H), 3.07-3.25(m, 3H), 3.63(s, 2H), 3.83(d, J=7.5Hz, 2H), 4.09(m, 1H), 4.90(m, 1H), 4.99(q, J=7.5Hz, 1H), 6.21(d, J=2.8Hz, 1H), 6.32(m, 1H), 6.58(d, J=7Hz, 1H), 7.05-7.37(m, 6H)

Example 136

Preparation of (s)-3-((s)-2-cycloheptylmethoxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-4-phenyl-

2-butanone (compd. No. 289 in Table 1)

mp: 77-79 °C

IR(KBr, cm^{-1}): 3350, 3300, 1718, 1690, 1660

5 NMR(CDCl_3 , δ): 0.89(d, J=6.0Hz, 3H), 0.91(d, J=6.1Hz, 3H), 1.10-1.90(m, 16H), 2.99(dd, J=6.7Hz, 15Hz, 1H), 3.08-3.25(m, 3H), 3.63(s, 2H), 3.87(d, J=5.8Hz, 2H), 4.12(m, 1H), 4.88(m, 1H), 4.99(q, J=6.7Hz, 1H), 6.18(d, J=3.1Hz, 1H), 6.29(m, 1H), 6.61(d, J=7Hz, 1H), 7.13(d, J=7.8Hz, 2H), 7.18-7.38(m, 4H)

Example 137

10

Preparation of (s)-3-[(s)-2-(3-cyclohexenyl)methoxycarbonylamino-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 293 in Table 1)

mp: 85-87 °C

15 IR(KBr, cm^{-1}): 3340, 3310, 1738, 1688, 1660

NMR(CDCl_3 , δ): 0.90(d, J=6.0Hz, 3H), 0.91(d, J=6.2Hz, 3H), 1.20-2.20(m, 10H), 3.01(dd, J=6.8Hz, 14Hz, 1H), 3.08-3.29(m, 3H), 3.63(s, 2H), 3.96(d, J=6.4Hz, 2H), 4.13(m, 1H), 4.92(m, 1H), 5.03(q, J=6.8Hz, 1H), 5.60-5.76(m, 2H), 6.19(d, J=2.9Hz, 1H), 6.29(m, 1H), 6.58(d, J=7Hz, 1H), 7.08-7.38(m, 6H)

20 Example 138

Preparation of (s)-3-[(s)-2-cyclohexyloxycarbonylamino-4-methylvaleryl-amino]-1-furfuryl thio-4-phenyl-2-butanone (compd. No. 296 in Table 1)

25 mp: 102-103 °C

IR(KBr, cm^{-1}): 3330, 3270, 1718, 1681, 1660

NMR(CDCl_3 , δ): 0.89(d, J=6.1Hz, 3H), 0.91(d, J=6.3Hz, 3H), 1.35-1.93(m, 13H), 3.01(dd, J=6.5Hz, 14Hz, 1H), 3.08-3.25(m, 3H), 3.63(s, 2H), 4.12(m, 1H), 4.62(m, 1H), 4.84(m, 1H), 5.01(q, J=6.5Hz, 1H), 6.18(d, J=2.9Hz, 1H), 6.29(m, 1H), 6.66(d, J=7Hz, 1H), 7.14(d, J=6.1Hz, 2H), 7.20-7.35(m, 4H)

30

Example 139

Preparation of (s)-3-[(s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-furfurylthio -4-phenyl-2-butanone (compd. No. 297 in Table 1)

35

mp: 103-105 °C

IR(KBr, cm^{-1}): 3350, 3300, 1725, 1690, 1658

40 NMR(CDCl_3 , δ): 0.90(d, J=6.2Hz, 6H), 1.30-1.65(m, 3H), 2.96(dd, J=7.0Hz, 14Hz, 1H), 3.07-3.28(m, 3H), 3.63(s, 2H), 4.13(m, 1H), 4.85-5.10(m, 2H), 5.09(s, 2H), 6.18(d, J=3.0Hz, 1H), 6.29(d, J=3.0Hz, 1H), 6.56(d, J=7Hz, 1H), 7.05-7.22(m, 11H)

Example 140

Preparation of (s)-3-[(R)-2-benzyloxycarbonylamino-4-methylvaleryl-amino]-1-furfurylthio -4-phenyl-2-butanone (compd. No. 297 in Table 1)

45

mp: 77-78 °C

IR(KBr, cm^{-1}): 3300, 1730, 1690, 1650

50 NMR(CDCl_3 , δ): 0.80-0.95(m, 6H), 1.20-1.70(m, 3H), 3.0(m, 1H), 3.12-3.20(m, 3H), 3.63(d, J=4.2Hz, 2H), 4.11(m, 1H), 4.95-5.10(m, 2H), 5.09(s, 2H), 6.19(d, J=2.9Hz, 1H), 6.28(m, 1H), 6.50(m, 1H), 7.07-7.40(m, 11H)

Example 141

Preparation of (s)-1-furfurylthio-3-[(s)-N-methyl -2-(benzyloxycarbonylamino)-4-methylvaleryl-amino]-4-phenyl-2-butanone (compd. No. 298 in Table 1)

55

IR(neat, cm^{-1}): 3320, 1720, 1650

NMR(CDCl_3 , δ): 0.85-0.98(m, 6H), 1.20-1.75(m, 3H), 2.80(s, 3H), 3.02(m, 1H), 3.08(d, J=15Hz, 1H), 3.23(d,

J=15Hz, 1H), 3.30(m, 1H), 3.65(s, 3H), 4.50(m, 1H), 4.74(m, 1H), 5.06(s, 2H), 5.20(d, J=8.5Hz, 1H), 6.18(d, J=3.1Hz, 1H), 6.30(m, 1H), 7.14-7.35(m, 11H)

Example 142

5

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(N-methylbenzyloxycarbonylamino)valeryl amino]-4-phenyl-2-butanone (compd. No. 299 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1695, 1650

10

NMR(CDCl_3 , δ): 0.85-0.95(m, 6H), 1.35-1.68(m, 3H), 2.54(s, 2H), 2.78(s, 1H), 2.80-2.98(m, 1H), 3.0-3.25(m, 3H), 3.64(s, 0.7H), 3.67(s, 1.3H), 4.50-4.75(m, 1H), 4.95(m, 1H), 5.13(s, 2H), 6.19(d, J=2.9Hz, 1H), 6.28(m, 1H), 6.55(d, J=7Hz, 0.7H), 6.95-7.40(m, 11.3H)

Example 143

15

Preparation of (s)-3-[(s)-2-(2-chlorobenzyloxycarbonylamino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 301 in Table 1)

mp: 80-85 °C

20

IR(KBr, cm^{-1}): 3340, 3290, 1735, 1698, 1660

NMR(CDCl_3 , δ): 0.83-0.98(m, 6H), 1.35-1.70(m, 3H), 2.98(dd, J=7.2Hz, 14Hz, 1H), 3.05-3.23(m, 3H), 3.63(s, 2H), 4.15(m, 1H), 4.93-5.03(m, 2H), 5.21(s, 2H), 6.17(d, J=3.2Hz, 1H), 6.29(m, 1H), 6.58(d, J=7Hz, 1H), 7.05-7.45(m, 10H)

25

Example 144

Preparation of (s)-3-[(s)-2-(4-chlorobenzyloxycarbonylamino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 303 in Table 1)

30

mp: 123-124 °C

IR(KBr, cm^{-1}): 3350, 3310, 1732, 1698, 1663

NMR(CDCl_3 , δ): 0.89(d, J=6.1Hz, 6H), 1.33-1.70(m, 3H), 2.98(dd, J=6.8Hz, 14Hz, 1H), 3.05-3.25(m, 3H), 3.63(s, 2H), 4.13(m, 1H), 4.90-5.12(m, 2H), 5.05(s, 2H), 6.19(d, J=3.2Hz, 1H), 6.27(m, 1H), 6.53(d, J=7Hz, 1H), 7.11(d, J=6.7Hz, 2H), 7.15-7.38(m, 8H)

35

Example 145

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(1,2,3,4-tetrahydro-1-naphthoxycarbonylamino)valeryl amino]-4-phenyl-2-butanone (compd. No. 308 in Table 1)

40

IR(KBr, cm^{-1}): 3300, 1715, 1675, 1655

NMR(CDCl_3 , δ): 0.85-1.0(m, 6H), 1.30-1.70(m, 3H), 1.70-2.10(m, 4H), 2.65-3.30(m, 6H), 3.64(s, 2H), 4.15(m, 1H), 4.89(d, J=7.6Hz, 1H), 5.01(m, 1H), 5.87(m, 1H), 6.20(d, J=3.1Hz, 1H), 6.30(m, 1H), 6.64(d, J=6.2Hz, 1H), 7.10-7.36(m, 10H)

45

Example 146

Preparation of (s)-3-[(s)-2-(9-fluorenylmethoxycarbonylamino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 309 in Table 1)

50

IR(KBr, cm^{-1}): 3320, 3280, 1680, 1660

NMR(CDCl_3 , δ): 0.83-0.98(m, 6H), 1.40-1.70(m, 3H), 2.98(m, 1H), 3.08-3.20(m, 3H), 3.62(s, 2H), 4.05-4.30(m, 2H), 4.30-4.50(m, 2H), 4.90-5.15(m, 2H), 6.18(m, 1H), 6.28(m, 1H), 6.52(m, 1H), 7.10-7.50(m, 10H), 7.58(d, J=7.3Hz, 2H), 7.77(d, J=7.3Hz, 2H)

55

Example 147

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-tetrahydrofurfuryloxycarbonylamino]valeryl amino]-4-phenyl

-2-butanone (compd. No. 310 in Table 1)

IR(neat, cm^{-1}): 3320, 1710, 1650

NMR(CDCl_3 , δ): 0.80-1.0(m, 6H), 1.20-1.70(m, 5H), 1.84-2.04(m, 2H), 2.98(dd, $J = 8.2\text{Hz}$, 15Hz, 1H), 3.10-3.25(m, 3H), 3.63(s, 2H), 3.66-4.0(m, 3H), 4.0-4.22(m, 3H), 4.96-5.08(m, 2H), 6.19(m, 1H), 6.29(m, 1H), 6.64(m, 1H), 7.15-7.40(m, 6H)

Example 148

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-tetrahydropyranylmethoxycarbonylamino)valerylamino]-4-phenyl-2-butanone (compd. No. 311 in Table 1)

IR(KBr, cm^{-1}): 3300, 1720, 1680, 1650

NMR(CDCl_3 , δ): 0.80-1.0(m, 6H), 1.23-1.90(m, 9H), 2.97(dd, $J = 7.3\text{Hz}$, 14Hz, 1H), 3.08-3.26(m, 3H), 3.38-3.70(m, 2H), 3.63(s, 2H), 3.90-4.17(m, 4H), 4.92-5.08(m, 2H), 6.19(m, 1H), 6.29(m, 1H), 6.62(d, $J = 7\text{Hz}$, 1H), 7.05-7.40(m, 6H)

Example 149

Preparation of (s)-3-((s)-2-furfuryloxycarbonylamino-4-methylvalerylamino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 312 in Table 1)

mp: 115-118 °C

IR(KBr, cm^{-1}): 3350, 3300, 1730, 1695, 1666

NMR(CDCl_3 , δ): 0.89(d, $J = 6.2\text{Hz}$, 6H), 1.28-1.65(m, 3H), 3.01(dd, $J = 6.5\text{Hz}$, 15Hz, 1H), 3.08-3.27(m, 3H), 3.63(s, 2H), 4.12(m, 1H), 4.86-5.07(m, 2H), 5.05(s, 2H), 6.19(d, $J = 2.9\text{Hz}$, 1H), 6.29(m, 1H), 6.36(m, 1H), 6.41(d, $J = 3.2\text{Hz}$, 1H), 6.54(m, 6H), 7.13(d, $J = 7.8\text{Hz}$, 2H), 7.18-7.32(m, 3H), 7.35(m, 1H), 7.42(s, 1H)

Example 150

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-pyridylmethoxycarbonylamino)valerylamino]-4-phenyl-2-butanone (compd. No. 313 in Table 1)

mp: 93-94 °C

IR(KBr, cm^{-1}): 3350, 3300, 1733, 1698, 1658

NMR(CDCl_3 , δ): 0.89(d, $J = 6.4\text{Hz}$, 3H), 0.91(d, $J = 6.1\text{Hz}$, 3H), 1.33-1.75(m, 3H), 2.98(dd, $J = 6.5\text{Hz}$, 14Hz, 1H), 3.08-3.27(m, 3H), 3.62(s, 2H), 4.14(m, 1H), 4.98(q, $J = 6.5\text{Hz}$, 1H), 5.10-5.30(m, 1H), 5.21(s, 2H), 6.17(d, $J = 3.2\text{Hz}$, 1H), 6.29(m, 1H), 6.65(d, $J = 7\text{Hz}$, 1H), 7.07-7.38(m, 8H), 7.72(t, $J = 8.3\text{Hz}$, 1H), 8.57(d, $J = 5.0\text{Hz}$, 1H)

Example 151

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(3-pyridylmethoxycarbonylamino)valerylamino]-4-phenyl-2-butanone (compd. No. 315 in Table 1)

IR(neat, cm^{-1}): 3320, 1720, 1698, 1600

NMR(CDCl_3 , δ): 0.90(d, $J = 6.2\text{Hz}$, 6H), 1.33-1.72(m, 3H), 2.98(dd, $J = 6.7\text{Hz}$, 14Hz, 1H), 3.08-3.27(m, 3H), 3.63(s, 2H), 4.12(m, 1H), 5.01(q, $J = 7.5\text{Hz}$, 1H), 5.0-5.20(m, 1H), 5.11(s, 2H), 6.19(d, $J = 3.0\text{Hz}$, 1H), 6.29(m, 1H), 6.53(m, 1H), 7.13(d, $J = 7.7\text{Hz}$, 2H), 7.18-7.37(m, 5H), 7.68(d, $J = 8\text{Hz}$, 1H), 8.52-8.63(m, 2H)

Example 152

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(4-pyridylmethoxycarbonylamino)valerylamino]-4-phenyl-2-butanone (compd. No. 317 in Table 1)

IR(neat, cm^{-1}): 3320, 1718, 1663

NMR(CDCl_3 , δ): 0.90-1.02(m, 6H), 1.36-1.75(m, 3H), 3.04(dd, $J = 6.7\text{Hz}$, 14Hz, 1H), 3.07-3.24(m, 3H), 3.63(s, 2H), 4.13(m, 1H), 5.03(g, $J = 6.7\text{Hz}$, 1H), 5.10(s, 2H), 5.30(d, $J = 7\text{Hz}$, 1H), 6.19(d, $J = 2.9\text{Hz}$, 1H), 6.29(m,

1H), 6.67(d, J=7Hz, 1H), 7.08-7.33(m, 7H), 7.35(m, 1H), 8.59(d, J=7.5Hz, 2H)

Example 153

- 5 Preparation of (s)-3-((s)-2-amino-4-methylvaleryl-amino)-1-furfurylthio-4-phenyl-2-butanone hydrochloride (compd. No. 323 in Table 1)

IR(KBr, cm^{-1}): 3400, 1700, 1655

- 10 NMR(D_2O , δ): 0.65-0.85(m, 6H), 1.30-1.50(m, 3H), 2.73(dd, J=9.2Hz, 14Hz, 1H), 3.02(dd, J=7.5Hz, 14Hz, 1H), 3.28(d, J=15Hz, 1H), 3.42(d, J=15Hz, 1H), 3.55(s, 2H), 3.73(m, 1H), 4.67(m, 1H), 6.08(d, J=2.8Hz, 1H), 6.20(m, 1H), 6.95-7.30(m, 5H), 7.28(m, 1H)

Example 154

- 15 Preparation of (s)-1-furfurylthio-3-((s)-2-isovaleryl-amino-4-methylvaleryl-amino)-4-phenyl-2-butanone (compd. No. 325 in Table 1)

mp: 108-115°C

IR(KBr, cm^{-1}): 3310, 1715, 1640

- 20 NMR(CDCl_3 , δ): 0.93-1.06(m, 12H), 1.40-1.75(m, 4H), 1.95-2.20(m, 2H), 2.98(dd, J=7.2Hz, 14Hz, 1H), 3.16(dd, J=6.7Hz, 14Hz, 1H), 3.16(s, 2H), 3.65(s, 2H), 4.43(m, 1H), 4.98(m, 1H), 5.70(d, J=7Hz, 1H), 6.18(d, J=2.6Hz, 1H), 6.29(m, 1H), 6.70(d, J=7Hz, 1H), 7.08-7.38(m, 6H)

Example 155

- 25 Preparation of (s)-3-[(s)-2-(3-cyclohexylpropionyl-amino)-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 328 in Table 1)

mp: 116-118°C

IR(KBr, cm^{-1}): 3300, 1722, 1710, 1638

- 30 NMR(CDCl_3 , δ): 0.80-1.0(m, 8H), 1.08-1.80(m, 14H), 2.15(t, J=7.8Hz, 2H), 2.98(dd, J=7.3Hz, 14Hz, 1H), 3.15(dd, J=5.3Hz, 14Hz, 1H), 3.16(s, 2H), 3.64(s, 2H), 4.40(m, 1H), 4.97(q, J=7.2Hz, 1H), 5.66(d, J=7Hz, 1H), 6.19(d, J=3.1Hz, 1H), 6.29(m, 1H), 6.66(d, J=7Hz, 1H), 7.13-7.38(m, 6H)

Example 156

- 35 Preparation of (s)-3-[(s)-2-(4-cyclohexylbutyryl-amino)-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 329 in Table 1)

IR(KBr, cm^{-1}): 3270, 1730, 1650, 1640

- 40 NMR(CDCl_3 , δ): 0.75-1.03(m, 8H), 1.03-1.75(m, 16H), 2.11(t, J=7.8Hz, 2H), 2.98(dd, J=7.2Hz, 14Hz, 1H), 3.11(dd, J=6.5Hz, 14Hz, 1H), 3.16(s, 2H), 3.64(s, 2H), 4.41(m, 1H), 4.98(m, 1H), 5.67(d, J=8Hz, 1H), 6.19(d, J=3.0Hz, 1H), 6.29(m, 1H), 6.69(d, J=7Hz, 1H), 7.10-7.37(m, 11H)

Example 157

- 45 Preparation of (s)-1-furfurylthio-3-[4-methyl-2-(3-phenylpropionyl-amino)valeryl-amino]-4-phenyl-2-butanone (compd. No. 331 in Table 1)

mp: 117-119°C

50 IR(KBr, cm^{-1}): 3320, 1730, 1710, 1643

- NMR(CDCl_3 , δ): 0.83(d, J=6.2Hz, 3H), 0.85(d, J=6.2Hz, 3H), 1.25-1.65(m, 3H), 2.33-2.53(m, 2H), 2.85-3.03(m, 3H), 3.05-3.18(m, 1H), 3.15(s, 2H), 3.64(s, 2H), 4.35(m, 1H), 4.96(q, J=6.7Hz, 1H), 5.53(d, J=7Hz, 1H), 6.19(d, J=3.3Hz, 1H), 6.30(m, 1H), 6.58(d, J=7Hz, 1H), 7.10-7.40(m, 11H)

Example 158

- Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(4-phenylbutyryl-amino)valeryl-amino]-4-phenyl-2-butanone (compd. No. 332 in Table 1)

mp: 106-108 °C

IR(KBr, cm⁻¹): 3300, 1728, 1708, 1638

NMR(CDCl₃, δ): 0.89(d, J = 5.9Hz, 3H), 0.91(d, J = 6.1Hz, 3H), 1.40-1.65(m, 3H), 1.85-2.05(m, 2H), 2.14(t, J = 7.4Hz, 2H), 2.63(t, J = 7.3Hz, 2H), 2.96(dd, J = 7.4Hz, 14Hz, 1H), 3.15(dd, J = 7.5Hz, 14Hz, 1H), 3.16(s, 2H), 3.63(s, 2H), 4.40(m, 1H), 4.98(d, J = 6.6Hz, 1H), 5.64(d, J = 7Hz, 1H), 6.18(d, J = 3.2Hz, 1H), 6.29(m, 1H), 6.63(d, J = 7Hz, 1H), 7.10-7.40(m, 11H)

Example 159

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(1-naphtylacetyl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 333 in Table 1)

mp: 143-146 °C

IR(KBr, cm⁻¹): 3300, 1715, 1650

NMR(CDCl₃, δ): 0.64(d, J = 6.8Hz, 3H), 0.66(d, J = 6.8Hz, 3H), 0.98-1.15(m, 2H), 1.25-1.45(m, 1H), 2.78(dd, J = 7.9Hz, 14Hz, 1H), 3.07(dd, J = 6.5Hz, 14Hz, 1H), 3.14(d, J = 1.7Hz, 2H), 3.64(s, 2H), 3.93(d, J = 16Hz, 1H), 4.04(d, J = 16Hz, 1H), 4.29(m, 1H), 4.86(m, 1H), 5.37(d, J = 7Hz, 1H), 6.19(d, J = 2.9Hz, 1H), 6.29(m, 1H), 6.53(d, J = 8Hz, 1H), 6.95-7.10(m, 2H), 7.20-7.30(m, 5H), 7.30-7.40(m, 2H), 7.45-7.60(m, 3H), 7.87(m, 1H)

Example 160

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-naphtylacetyl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 334 in Table 1)

mp: 123-125 °C

IR(KBr, cm⁻¹): 3320, 3300, 1715, 1640

NMR(CDCl₃, δ): 0.73-0.90(m, 6H), 1.20-1.70(m, 3H), 2.91(dd, J = 7.7Hz, 14Hz, 1H), 3.09(dd, J = 7.7Hz, 14Hz, 1H), 3.14(s, 2H), 3.63(s, 2H), 3.69(d, J = 3.1Hz, 2H), 4.37(m, 1H), 4.93(m, 1H), 5.60(d, J = 8.3Hz, 1H), 6.18(d, J = 3.1Hz, 1H), 6.28(m, 1H), 6.62(d, J = 7.5Hz, 1H), 7.05-7.16(m, 2H), 7.20-7.35(m, 5H), 7.45-7.55(m, 2H), 7.67(s, 1H), 7.74-7.90(m, 3H)

Example 161

Preparation of (s)-3-[(s)-2-cinnamoyl amino-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 335 in Table 1)

mp: 141-143 °C

IR(KBr, cm⁻¹): 3300, 1730, 1710, 1650, 1623

NMR(CDCl₃, δ): 0.93(d, J = 4.3Hz, 6H), 1.43-1.78(m, 3H), 2.95(dd, J = 7.5Hz, 15Hz, 1H), 3.15(dd, J = 7.5Hz, 15Hz, 1H), 3.19(s, 2H), 3.65(s, 2H), 4.59(m, 1H), 5.0(q, J = 6.6Hz, 1H), 5.94(d, J = 8Hz, 1H), 6.19(d, J = 3.3Hz, 1H), 6.29(m, 1H), 6.35(d, J = 16Hz, 1H), 6.82(d, J = 8Hz, 1H), 7.10-7.30(m, 5H), 7.30-7.45(m, 4H), 7.45-7.55(m, 2H), 7.63(d, J = 16Hz, 1H)

Example 162

Preparation of (s)-3-[(s)-2-(3-benzothiényl acetyl amino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 345 in Table 1)

mp: 150-153 °C

IR(KBr, cm⁻¹): 3300, 1710, 1640

NMR(CDCl₃, δ): 0.65-0.80(m, 6H), 1.13-1.28(m, 2H), 1.35-1.55(m, 1H), 2.83(dd, J = 7.7Hz, 18Hz, 1H), 3.07-(dd, J = 7.7Hz, 18Hz, 1H), 3.14(s, 2H), 3.63(s, 2H), 3.78(s, 2H), 4.30-4.45(m, 1H), 4.59(q, J = 6.7Hz, 1H), 5.68-(d, J = 8Hz, 1H), 6.18(d, J = 3.2Hz, 1H), 6.27-6.34(m, 1H), 6.63(d, J = 8Hz, 1H), 7.05-7.15(m, 2H), 7.20-7.48-(m, 7H), 7.65-7.78(m, 1H), 7.85-7.97(m, 1H)

Example 163

Preparation of (s)-3-[(s)-2-cyclohexyloxyacetyl amino-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-

butanone (compd. No. 347 in Table 1)

IR(neat, cm^{-1}): 3300, 1700, 1650

NMR(CDCl_3 , δ): 0.87-0.92(m, 6H), 1.18-1.90(m, 13H), 2.97(dd, $J=7.6\text{Hz}$, 14Hz, 1H), 3.14(dd, $J=6.3\text{Hz}$, 14Hz, 1H), 3.14(d, $J=15\text{Hz}$, 1H), 3.21(d, $J=15\text{Hz}$, 1H), 3.28(m, 1H), 3.64(s, 2H), 3.86(d, $J=16\text{Hz}$, 1H), 3.95-
5 (d, $J=16\text{Hz}$, 1H), 4.39(m, 1H), 4.97(q, $J=7.5\text{Hz}$, 1H), 6.19(d, $J=2.9\text{Hz}$, 1H), 6.29(m, 1H), 6.76(d, $J=8\text{Hz}$, 1H), 6.80(d, $J=8\text{Hz}$, 1H), 7.13-7.36(m, 6H)

Example 164

10

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-phenoxyacetylaminovaleryl amino]-4-phenyl-2-butanone (compd. No. 348 in Table 1)

mp: 91-95 °C

15 IR(KBr, cm^{-1}): 3300, 3270, 1735, 1650

NMR(CDCl_3 , δ): 0.80-0.95(m, 6H), 1.30-1.75(m, 3H), 2.95(dd, $J=7.7\text{Hz}$, 14Hz, 1H), 3.14(dd, $J=6.4\text{Hz}$, 14Hz, 1H), 3.19(d, $J=1.9\text{Hz}$, 2H), 3.66(s, 2H), 4.39(d, $J=15\text{Hz}$, 1H), 4.47(m, 1H), 4.49(d, $J=15\text{Hz}$, 1H), 5.0(q, $J=7.4\text{Hz}$, 1H), 6.20(d, $J=2.9\text{Hz}$, 1H), 6.29(m, 1H), 6.60(d, $J=7\text{Hz}$, 1H), 6.73(d, $J=8\text{Hz}$, 1H), 6.91(d, $J=8.8\text{Hz}$, 2H), 7.0-7.36(m, 9H)

20

Example 165

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-phenoxypropionyl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 349 in Table 1)

25

IR(KBr, cm^{-1}): 3280, 1710, 1640

NMR(CDCl_3 , δ): 0.75(d, $J=6.5\text{Hz}$, 3H), 0.89(d, $J=6.6\text{Hz}$, 1.5H), 0.91(d, $J=6.6\text{Hz}$, 1.5H), 1.05-1.70(m, 6H), 2.76(dd, $J=7.9\text{Hz}$, 14Hz, 0.5H), 2.93-3.20(m, 3.5H), 3.64(s, 2H), 4.37(m, 1H), 4.67(m, 1H), 4.87(q, $J=7.3\text{Hz}$, 0.5H), 4.99(q, $J=7.3\text{Hz}$, 0.5H), 6.19(m, 1H), 6.29(m, 1H), 6.42(d, $J=8\text{Hz}$, 0.5H), 6.62-6.67(m, 1.5H), 6.86-
30 6.93(m, 2H), 6.99-7.06(m, 2H), 7.13-7.36(m, 7H)

Example 166

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-phenoxybutyryl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 350 in Table 1)

35

IR(KBr, cm^{-1}): 3260, 1720, 1705, 1640

NMR(CDCl_3 , δ): 0.73(d, $J=6.5\text{Hz}$, 3H), 0.80-0.96(m, 3H), 0.96-1.10(m, 3H), 1.20-1.65(m, 3H), 1.75-2.05(m, 2H), 2.73(dd, $J=8.1\text{Hz}$, 14Hz, 0.5H), 2.86-3.20(m, 1.5H), 3.14(s, 2H), 3.63(s, 2H), 4.37(m, 1H), 4.53(m, 1H),
40 4.85(q, $J=5.0\text{Hz}$, 0.5H), 4.99(q, $J=5.0\text{Hz}$, 0.5H), 6.19(m, 1H), 6.29(m, 1H), 6.43(d, $J=8\text{Hz}$, 0.5H), 6.52(d, $J=8\text{Hz}$, 0.5H), 6.55(d, $J=8\text{Hz}$, 0.5H), 6.64(d, $J=8\text{Hz}$, 0.5H), 6.84-6.96(m, 2H), 6.96-7.05(m, 2H), 7.05-7.40-
(m, 7H)

Example 167

45

Preparation of (s)-3-[(s)-2-(2-chlorophenoxyacetyl amino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 354 in Table 1)

mp: 99-102 °C

50 IR(KBr, cm^{-1}): 3300, 1710, 1670, 1640

NMR(CDCl_3 , δ): 0.85-0.95(m, 6H), 1.42-1.75(m, 3H), 2.97(dd, $J=7.5\text{Hz}$, 14Hz, 1H), 3.16(dd, $J=5.3\text{Hz}$, 14Hz, 1H), 3.16(d, $J=15\text{Hz}$, 1H), 3.23(d, $J=15\text{Hz}$, 1H), 3.65(s, 2H), 4.24(m, 1H), 4.43(d, $J=15\text{Hz}$, 1H), 4.51(d, $J=15\text{Hz}$, 1H), 5.02(q, $J=7.5\text{Hz}$, 1H), 6.19(d, $J=2.9\text{Hz}$, 1H), 6.29(m, 1H), 6.67(d, $J=8\text{Hz}$, 1H), 6.88(d, $J=8\text{Hz}$, 1H), 6.95-7.45(m, 10H)

55

Example 168

Preparation of (s)-3-[(s)-2-(4-chlorophenoxyacetyl amino)-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-

butanone (compd. No. 356 in Table 1)

mp: 116-117 °C

IR(KBr, cm^{-1}): 3300, 3250, 1730, 1670, 1650

- 5 NMR(CDCl_3 , δ): 0.83-0.96(m, 6H), 1.45-1.70(m, 3H), 2.96(dd, $J = 7.6\text{Hz}$, 14Hz, 1H), 3.11(dd, $J = 6.4\text{Hz}$, 14Hz, 1H), 3.19(s, 2H), 3.66(s, 2H), 4.35(d, $J = 15\text{Hz}$, 1H), 4.46(d, $J = 15\text{Hz}$, 1H), 4.44(m, 1H), 5.01(dd, $J = 7.5\text{Hz}$, 14Hz, 1H), 6.20(m, 1H), 6.30(m, 1H), 6.58(d, $J = 8\text{Hz}$, 1H), 6.71(d, $J = 9\text{Hz}$, 1H), 6.80-6.86(m, 2H), 7.11-7.36(m, 8H)

10 Example 169

Preparation of (s)-1-furfurylthio-3-[(s)-2-(2-methoxyphenoxyacetyl amino)-4-methylvaleryl amino]-4-phenyl 1-2-butanone (compd. No. 361 in Table 1)

- 15 IR(KBr, cm^{-1}): 3280, 1705, 1665, 1645

NMR(CDCl_3 , δ): 0.87(d, $J = 6.7\text{Hz}$, 3H), 0.89(d, $J = 6.7\text{Hz}$, 3H), 1.39-1.71(m, 3H), 2.91(dd, $J = 7.7\text{Hz}$, 14Hz, 1H), 3.10(dd, $J = 7.7\text{Hz}$, 14Hz, 1H), 3.13(d, $J = 17\text{Hz}$, 1H), 3.21(d, $J = 17\text{Hz}$, 1H), 3.64(s, 2H), 3.86(s, 2H), 4.42(m, 1H), 4.45(d, $J = 15\text{Hz}$, 1H), 4.55(d, $J = 15\text{Hz}$, 1H), 4.95(q, $J = 6.4\text{Hz}$, 1H), 4.85-5.05(m, 1H), 6.20(m, 1H), 6.29(m, 1H), 6.70(d, $J = 7.1\text{Hz}$, 1H), 6.90-7.0(m, 3H), 7.0-7.40(m, 7H)

20

Example 170

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(1-naphthoxyacetyl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 364 in Table 1)

25

mp: 118-120 °C

IR(KBr, cm^{-1}): 3300, 1730, 1670, 1650

- 30 NMR(CDCl_3 , δ): 0.75-1.03(m, 6H), 1.38-1.65(m, 3H), 2.95(dd, $J = 7.8\text{Hz}$, 14Hz, 1H), 3.15(dd, $J = 6.4\text{Hz}$, 14Hz, 1H), 3.19(s, 2H), 3.66(s, 2H), 4.50(m, 1H), 4.61(d, $J = 15\text{Hz}$, 1H), 4.69(d, $J = 15\text{Hz}$, 1H), 5.04(q, $J = 7.0\text{Hz}$, 1H), 6.20(d, $J = 3.1\text{Hz}$, 1H), 6.29(m, 1H), 6.62(d, $J = 7.1\text{Hz}$, 1H), 6.70-6.90(m, 2H), 7.0-7.65(m, 10H), 7.84(m, 1H), 8.18(m, 1H)

Example 171

- 35 Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-naphthoxyacetyl amino)valeryl amino]-4-phenyl-2-butanone (compd. No. 365 in Table 1)

IR(KBr, cm^{-1}): 3300, 1710, 1675, 1650

- 40 NMR(CDCl_3 , δ): 0.86(d, $J = 6.1\text{Hz}$, 6H), 1.45-1.70(m, 3H), 2.95(dd, $J = 7.6\text{Hz}$, 14Hz, 1H), 3.12(dd, $J = 6.5\text{Hz}$, 14Hz, 1H), 3.18(d, $J = 1.8\text{Hz}$, 2H), 3.66(s, 2H), 4.50(m, 1H), 4.52(d, $J = 15\text{Hz}$, 1H), 4.61(d, $J = 15\text{Hz}$, 1H), 5.0(q, $J = 6.5\text{Hz}$, 1H), 6.20(m, 1H), 6.29(m, 1H), 6.62(d, $J = 8\text{Hz}$, 1H), 6.79(d, $J = 8.5\text{Hz}$, 1H), 7.10-7.30(m, 7H), 7.30-7.52(m, 3H), 7.70-7.90(m, 3H)

Example 172

45

Preparation of (s)-3-[(s)-2-benzyloxyacetyl amino-4-methylvaleryl amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 366 in Table 1)

IR(KBr, cm^{-1}): 3350, 3310, 1690, 1640

- 50 NMR(CDCl_3 , δ): 0.89(d, $J = 5.7\text{Hz}$, 3H), 0.91(d, $J = 5.7\text{Hz}$, 3H), 1.46-1.70(m, 3H), 2.96(dd, $J = 7.7\text{Hz}$, 14Hz, 1H), 3.14(dd, $J = 6.4\text{Hz}$, 14Hz, 1H), 3.17(d, $J = 2.7\text{Hz}$, 2H), 3.64(s, 2H), 3.88(d, $J = 14\text{Hz}$, 1H), 3.96(d, $J = 14\text{Hz}$, 1H), 4.41(m, 1H), 4.55(s, 2H), 4.98(q, $J = 6.6\text{Hz}$, 1H), 6.19(m, 1H), 6.29(m, 1H), 6.69(d, $J = 8\text{Hz}$, 1H), 6.78(d, $J = 8\text{Hz}$, 1H), 7.10-7.42(m, 11H)

55 Example 173

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl -2-(2-tetrahydropyranyloxyacetyl amino)valeryl amino]-4-phenyl 1-2-butanone (compd. No. 370 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1660

NMR(CDCl_3 , δ): 0.85-0.95(m, 6H), 1.40-1.88(m, 9H), 2.97(m, 1H), 3.13(m, 1H), 3.19(m, 2H), 3.50(m, 1H), 3.64(s, 2H), 3.78(m, 1H), 3.91-4.20(m, 2H), 4.42(m, 1H), 4.55(m, 1H), 4.97(m, 1H), 6.19(m, 1H), 6.29(m, 1H), 6.30-6.85(m, 2H), 7.10-7.36(m, 6H)

5

Example 174

Preparation of (s)-3-[(s)-2-(2-benzofuranylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 382 in Table 1)

10

IR(KBr, cm^{-1}): 3300, 1720, 1640

NMR(CDCl_3 , δ): 0.90-1.0(m, 6H), 1.55-1.80(m, 3H), 2.97(dd, $J = 7.6\text{Hz}$, 14Hz, 1H), 3.13(dd, $J = 6.4\text{Hz}$, 14Hz, 1H), 3.20(s, 2H), 3.66(s, 2H), 4.63(m, 1H), 5.04(q, $J = 7.4\text{Hz}$, 1H), 6.20(m, 1H), 6.29(m, 1H), 6.68(d, $J = 8\text{Hz}$, 1H), 6.82(d, $J = 8\text{Hz}$, 1H), 7.02-7.20(m, 5H), 7.27-7.36(m, 2H), 7.40-7.55(m, 3H), 7.70(d, $J = 7.9\text{Hz}$, 1H)

15

Example 175

Preparation of (s)-3-[(s)-2-(2-chromanylcarbonylamino)-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 384 in Table 1)

20

IR(KBr, cm^{-1}): 3300, 1730, 1650

NMR(CDCl_3 , δ): 0.78-0.85(m, 3H), 0.93(d, $J = 6.3\text{Hz}$, 1.5H), 0.95(d, $J = 6.3\text{Hz}$, 1.5H), 1.22-1.78(m, 3H), 1.78-2.15(m, 1H), 2.28-2.45(m, 1H), 2.66-3.13(m, 4H), 3.13-3.20(m, 2H), 3.63(s, 1H), 3.65(s, 1H), 4.35-4.54(m, 2H), 4.90-5.08(m, 1H), 6.18-6.22(m, 1H), 6.30-6.34(m, 1H), 6.51(d, $J = 8\text{Hz}$, 0.5H), 6.70(d, $J = 8\text{Hz}$, 0.5H), 6.76(d, $J = 9\text{Hz}$, 0.5H), 6.83(d, $J = 8\text{Hz}$, 0.5H), 6.87-6.94(m, 2H), 7.04-7.36(m, 8H)

25

Example 176

Preparation of (s)-1-furfurylthio-3-[(s)-4-methyl-2-(4-oxo-4H-1-benzopyran-2-ylcarbonylamino)valeryl-amino]-4-phenyl-2-butanone (compd. No. 386 in Table 1)

30

IR(neat, cm^{-1}): 3320, 1710, 1650

NMR(CDCl_3 , δ): 0.95-0.98(m, 6H), 1.62-1.80(m, 3H), 2.98(dd, $J = 7.5\text{Hz}$, 14Hz, 1H), 3.16(dd, $J = 6.4\text{Hz}$, 14Hz, 1H), 3.21(s, 2H), 3.64(s, 1H), 4.62(m, 1H), 5.08(q, $J = 6.6\text{Hz}$, 1H), 6.20(m, 1H), 6.30(m, 1H), 6.56(d, $J = 8\text{Hz}$, 1H), 7.06-7.26(m, 7H), 7.36(m, 1H), 7.44-7.60(m, 2H), 7.70-7.82(m, 1H), 8.24(dd, $J = 1.7\text{Hz}$, 7.9Hz, 1H)

35

Example 177

Preparation of (s)-3-[(s)-2-(3-benzylureido)-4-methylvaleryl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 388 in Table 1)

40

mp: 95-97 °C

IR(KBr, cm^{-1}): 3310, 1708, 1650, 1628

NMR(CDCl_3 , δ): 0.87(d, $J = 4.9\text{Hz}$, 6H), 1.30-1.70(m, 3H), 2.93(dd, $J = 6.5\text{Hz}$, 14Hz, 1H), 2.98-3.19(m, 3H), 3.58(s, 2H), 4.17-4.45(m, 3H), 4.87(q, $J = 6.5\text{Hz}$, 1H), 5.17-5.35(m, 2H), 6.16(d, $J = 3.1\text{Hz}$, 1H), 6.28(m, 1H), 6.95-7.38(m, 12H)

45

Example 178

Preparation of (s)-3-[(s)-2-benzoyloxy-carbonylamino-3-cyclohexylpropionyl-amino]-1-furfurylthio-4-phenyl-2-butanone (compd. No. 400 in Table 1)

50

mp: 124-125 °C

IR(KBr, cm^{-1}): 3350, 3310, 1735, 1690, 1655

NMR(CDCl_3 , δ): 0.78-1.0(m, 2H), 1.0-1.45(m, 6H), 1.45-1.80(m, 5H), 2.83-3.24(m, 4H), 3.62(s, 2H), 4.16(m, 1H), 4.99(q, $J = 6.8\text{Hz}$, 1H), 5.10(s, 2H), 4.95-5.07(m, 1H), 6.18(d, $J = 2.8\text{Hz}$, 1H), 6.29(m, 1H), 6.58(m, 1H), 7.03-7.42(m, 11H)

55

Example 179

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-3-phenylpropionylamino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 401 in Table 1)

5 IR(KBr, cm^{-1}): 3300, 3260, 1725, 1685, 1650

NMR(CDCl_3 , δ): 2.91(dd, $J = 7.1\text{Hz}$, 14Hz, 1H), 2.95-3.10(m, 5H), 3.56(s, 2H), 4.37(m, 1H), 4.95(q, $J = 7.4\text{Hz}$, 1H), 5.08(s, 2H), 5.13(m, 1H), 6.17(d, $J = 2.5\text{Hz}$, 1H), 6.29(m, 1H), 6.32(d, $J = 7\text{Hz}$, 1H), 7.0-7.04(m, 2H), 7.10-7.35(m, 14H)

10 Example 180

Preparation of (s)-3-(2-benzoylamino-2-methoxyacetyl-amino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 404 in Table 1)

15 IR(KBr, cm^{-1}): 3300, 1730, 1670, 1640

NMR(CDCl_3 , δ): 3.04(dd, $J = 7.0\text{Hz}$, 14Hz, 1H), 3.11-3.22(m, 3H), 3.45(s, 0.9H), 3.49(s, 2.1H), 3.65(s, 0.6H), 3.68(s, 1.4H), 5.09(m, 1H), 5.66(d, $J = 8\text{Hz}$, 0.7H), 5.67(d, $J = 8\text{Hz}$, 0.3H), 6.20(m, 1H), 6.30(m, 1H), 6.87(d, $J = 8\text{Hz}$, 0.3H), 7.03(d, $J = 8\text{Hz}$, 0.7H), 7.08-7.28(m, 7H), 7.41-7.60(m, 3H), 7.78-7.86(m, 2H)

20 Example 181

Preparation of (s)-3-(2-benzyloxycarbonylamino-2-isopropoxyacetyl-amino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 405 in Table 1)

25 IR(KBr, cm^{-1}): 3300, 1720, 1695, 1655

NMR(CDCl_3 , δ): 1.05-1.24(m, 6H), 2.98-3.20(m, 2H), 3.13(s, 1H), 3.21(s, 1H), 3.63(s, 1H), 3.65(s, 1H), 3.96(m, 1H), 4.99(m, 1H), 5.13(s, 2H), 5.35(m, 1H), 5.40(d, $J = 7\text{Hz}$, 0.5H), 5.57(d, $J = 7\text{Hz}$, 0.5H), 6.19(m, 1H), 6.29(m, 1H), 7.07-7.40(m, 12H)

30 Example 182

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(5-methoxycarbonylfurfurylthio)-4-phenyl-2-butanone (compd. No. 413 in Table 1)

35 mp: 85-93 °C

IR(KBr, cm^{-1}): 3300, 1740-1680, 1658

NMR(CDCl_3 , δ): 0.89(d, $J = 6.3\text{Hz}$, 6H), 1.25-1.65(m, 3H), 2.86-3.03(m, 1H), 3.05-3.38(m, 2H), 3.42(d, $J = 14\text{Hz}$, 1H), 3.65(s, 2H), 3.87(s, 3H), 4.08-4.23(m, 1H), 4.95-5.15(m, 4H), 6.31(d, $J = 3.5\text{Hz}$, 1H), 6.85-6.95(m, 1H), 7.09(d, $J = 3.5\text{Hz}$, 1H), 7.13-7.45(m, 10H)

40

Example 183

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(5-chloro-2-thienylmethylthio)-4-phenyl-2-butanone (compd. No. 423 in Table 1)

45

mp: 105-107 °C

IR(KBr, cm^{-1}): 3340, 3310, 1728, 1692, 1650

NMR(CDCl_3 , δ): 0.90-1.0(m, 6H), 1.30-1.65(m, 3H), 2.90-3.23(m, 4H), 3.70(s, 2H), 4.13(m, 1H), 4.85-5.0(m, 2H), 5.09(s, 2H), 6.53(m, 1H), 6.60-6.73(m, 2H), 7.12(d, $J = 6.0\text{Hz}$, 2H), 7.15-7.40(m, 8H)

50

Example 184

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-phenyl-1-(2-pyridylmethylthio)-2-butanone (compd. No. 428 in Table 1)

55

mp: 82-87 °C

IR(KBr, cm^{-1}): 3330, 3280, 1718, 1680, 1655

NMR(CDCl_3 , δ): 0.89(d, $J = 6.2\text{Hz}$, 6H), 1.30-1.70(m, 3H), 2.98(dd, $J = 4.8\text{Hz}$, 14Hz, 1H), 3.14(dd, $J = 4.8\text{Hz}$,

14Hz, 1H), 3.16(d, J=15Hz, 1H), 3.31(d, J=15Hz, 1H), 3.75(s, 2H), 4.13(m, 1H), 5.0(q, J=7.4Hz, 1H), 5.08(s, 2H), 4.93-5.15(m, 1H), 6.74(d, J=7Hz, 1H), 7.10-7.42(m, 12H), 7.65(dt, J=1.8Hz, 7.7Hz, 1H), 8.52(d, J=4.9Hz, 1H)

5 Example 185

Preparation of (s)-1-(2-benzimidazolymethylthio)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-phenyl-2-butanone (compd. No. 434 in Table 1)

10 mp: 125-129 °C

IR(KBr, cm⁻¹): 3300, 1710, 1690, 1653

NMR(CDCl₃, δ): 0.80-1.0(m, 6H), 1.30-1.70(m, 3H), 2.75-2.95(m, 1H), 2.95-3.25(m, 2H), 3.25-3.55(m, 1H), 3.73-4.08(m, 2H), 4.10-4.25(m, 1H), 4.90-5.25(m, 2H), 5.07(s, 2H), 7.0-7.15(m, 2H), 7.15-7.40(m, 12H), 7.40-7.70(m, 2H)

15

Example 186

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(3,5-dimethyl-4-isooxazolyl-methylthio)-4-phenyl-2-butanone (compd. No. 438 in Table 1)

20

IR(neat, cm⁻¹): 3320, 1720, 1705, 1655

NMR(CDCl₃, δ): 0.90(d, J=5.8Hz, 6H), 1.30-1.65(m, 3H), 2.24(s, 3H), 2.34(s, 3H), 2.90-3.10(m, 4H), 3.35(s, 2H), 4.12(m, 1H), 4.93-5.13(m, 2H), 5.09(s, 2H), 6.63(d, J=8Hz, 1H), 7.10-7.45(m, 10H)

25 Example 187

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(2-methyl-4-thiazolylmethylthio)-4-phenyl-2-butanone (compd. No. 443 in Table 1)

30 IR(neat, cm⁻¹): 3330, 1725, 1705, 1660

NMR(CDCl₃, δ): 0.89(d, J=5.9Hz, 6H), 1.30-1.70(m, 3H), 2.68(s, 3H), 2.95-3.07(m, 1H), 3.07-3.30(m, 3H), 3.69(s, 2H), 4.05-4.20(m, 1H), 4.93-5.20(m, 2H), 5.09(s, 2H), 6.58-6.78(m, 1H), 6.94(s, 1H), 7.08-7.50(m, 10H)

35 Example 188

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(2-oxo-4-oxazolidinylmethylthio)-4-phenyl-2-butanone (compd. No. 445 in Table 1)

40 IR(neat, cm⁻¹): 3330, 1705, 1695, 1655

NMR(CDCl₃, δ): 0.78-0.95(m, 6H), 1.20-1.75(m, 3H), 2.40-2.62(m, 2H), 2.93(m, 1H), 3.01-3.22(m, 2H), 3.37(m, 1H), 3.84(m, 1H), 3.99(m, 1H), 4.12(m, 1H), 4.38(m, 1H), 4.92(m, 1H), 5.09(s, 2H), 5.56(d, J=7Hz, 1H), 6.42(s, 1H), 6.95-7.22(m, 11H)

45 Example 189

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methoxy-4-phenyl-2-butanone (compd. No. 447 in Table 1)

50 mp: 87-92 °C

IR(KBr, cm⁻¹): 3340, 3285, 1739, 1688, 1657

NMR(CDCl₃, δ): 0.90(d, J=6.2Hz, 6H), 1.30-1.75(m, 3H), 2.90-3.10(m, 2H), 3.35(s, 3H), 3.87(d, J=18Hz, 1H), 4.08(d, J=18Hz, 1H), 4.13(m, 1H), 4.96(m, 1H), 5.06(m, 1H), 5.09(s, 2H), 6.57(m, 1H), 7.11(d, J=7.4Hz, 2H), 7.10-7.33(m, 3H), 7.35(s, 5H)

55

Example 190

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-dimethyl-amino-4-phenyl-2-

butanone (compd. No. 465 in Table 1)

mp: 81-82 °C

IR(KBr, cm^{-1}): 3330, 3295, 1730, 1683, 1653

5 NMR(CDCl_3 , δ): 0.75-1.0(m, 6H), 1.30-1.70(m, 3H), 2.18(s, 3H), 2.21(s, 3H), 2.80-3.15(m, 3H), 3.25(t, $J=19\text{Hz}$, 1H), 4.14(m, 1H), 4.91(m, 1H), 5.08(s, 2H), 5.15-5.35(m, 1H), 6.70-6.90(m, 1H), 7.05-7.18(m, 2H), 7.18-7.30(m, 3H), 7.30-7.40(m, 5H)

Example 191

10

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(N-methylfurfurylamino)-4-phenyl-2-butanone (compd. No. 479 in Table 1)

IR(KBr, cm^{-1}): 3320, 1728, 1685, 1550

15 NMR(CDCl_3 , δ): 0.85-1.0(m, 6H), 1.25-1.80(m, 3H), 2.25(s, 3H), 2.75-2.95(m, 1H), 2.95-3.15(m, 2H), 3.28-3.45(m, 1H), 3.45-3.70(m, 2H), 4.15(m, 1H), 4.87-5.15(m, 2H), 5.09(s, 2H), 6.18(d, $J=2.8\text{Hz}$, 1H), 6.29(dd, $J=3.1\text{Hz}$, 1.9Hz, 1H), 6.55-6.75(m, 1H), 7.03-7.15(m, 2H), 7.15-7.25(m, 3H), 7.25-7.40(m, 6H)

Example 192

20

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-(4-methyl-1-piperazyl)-4-phenyl-2-butanone (compd. No. 488 in Table 1)

mp: 99-100 °C

25 IR(KBr, cm^{-1}): 3320, 1733, 1696, 1655

NMR(CDCl_3 , δ): 0.87-1.0(m, 6H), 1.30-1.70(m, 3H), 2.27(s, 3H), 2.30-2.50(m, 8H), 2.85-3.10(m, 3H), 3.10-3.33(m, 1H), 4.10(m, 1H), 4.99(q, $J=7.4\text{Hz}$, 1H), 5.09(s, 2H), 5.0-5.20(m, 1H), 6.60-6.90(m, 1H), 7.15(d, $J=7.0\text{Hz}$, 2H), 7.18-7.30(m, 3H), 7.30-7.40(m, 5H)

Example 193

3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(4-fluorophenyl)-1-furfurylthio-2-butanone (compd. No. 496 in Table 1)

35 mp: 101 °C

IR(KBr, cm^{-1}): 3300, 1720, 1680, 1650

NMR(CDCl_3 , δ): 0.82-0.99(m, 6H), 1.23-1.75(m, 3H), 2.82-3.02(m, 1H), 3.05-3.25(m, 3H), 3.65(s, 2H), 4.05-4.18(m, 1H), 4.90-5.02(m, 2H), 5.07(s, 2H), 6.21(d, $J=3.0\text{Hz}$, 1H), 6.28(m, 1H), 6.50-6.55(m, 1H), 6.87-7.0(m, 2H), 7.03-7.15(m, 2H), 7.25-7.40(m, 6H)

40

Example 194

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(2-chlorophenyl)-1-furfurylthio-2-butanone (compd. No. 503 in Table 1)

45

mp: 110 °C

IR(KBr, cm^{-1}): 3300, 1735, 1690, 1660

50 NMR(CDCl_3 , δ): 0.86(d, $J=6.0\text{Hz}$, 3H), 0.88(d, $J=6.0\text{Hz}$, 3H), 1.21-1.80(m, 3H), 2.97-3.12(m, 1H), 3.19-3.38(m, 1H), 3.28(s, 2H), 3.67(s, 2H), 4.10(m, 1H), 4.90-5.07(m, 2H), 5.09(d, $J=3.9\text{Hz}$, 2H), 6.21(d, $J=2.8\text{Hz}$, 1H), 6.30(m, 1H), 6.63(m, 1H), 7.08-7.20(m, 5H), 7.30-7.51(m, 5H)

Example 195

55 Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(4-chlorophenyl)-1-methylthio-2-butanone (compd. No. 506 in Table 1)

mp: 119-121 °C

IR(KBr, cm^{-1}): 3320, 3280, 1703, 1685, 1658

NMR(CDCl₃, δ): 0.80-1.0(m, 6H), 1.30-1.65(m, 3H), 1.99(s, 3H), 2.93(dd, J=7.0Hz, 15Hz, 1H), 3.05-3.35(m, 3H), 4.15(m, 1H), 4.90-5.22(m, 2H), 5.10(s, 2H), 5.62(d, J=7Hz, 1H), 7.07(d, J=8.2Hz, 2H), 7.23(d, J=8.2Hz, 2H), 7.36(s, 5H)

5 Example 196

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(4-chlorophenyl)-1-furfurylthio-4-butanone (compd. No. 508 in Table 1)

10 IR(KBr, cm⁻¹): 3300, 3270, 1705, 1685, 1645

NMR(CDCl₃, δ): 0.82-0.95(m, 6H), 1.30-1.66(m, 3H), 2.93(m, 1H), 3.05-3.15(m, 3H), 3.64(s, 2H), 4.10(m, 1H), 4.90-5.05(m, 2H), 5.10(s, 2H), 6.19(m, 1H), 6.30(m, 1H), 6.57(m, 1H), 7.06(d, J=8.2Hz, 2H), 7.18-7.30(m, 3H), 7.30-7.40(m, 5H)

15 Example 197

Preparation of (s)-4-(4-chlorophenyl)-1-furfurylthio-3-((s)-4-methyl-2-phenoxyacetyl-amino valeryl-amino)-2-butanone (compd. No. 511 in Table 1)

20 IR(KBr, cm⁻¹): 3280, 1720, 1645

NMR(CDCl₃, δ): 0.80-0.95(m, 6H), 1.38-1.70(m, 3H), 2.90(dd, J=7.3Hz, 14Hz, 1H), 3.10-3.23(m, 3H), 3.66(s, 2H), 4.35-4.53(m, 3H), 4.97(m, 1H), 6.20(m, 1H), 6.30(m, 1H), 6.63(d, J=7Hz, 1H), 6.73(d, J=8Hz, 1H), 7.88-7.95(m, 2H), 7.0-7.15(m, 3H), 7.20-7.40(m, 5H)

25 Example 198

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(4-methoxyphenyl)-1-methylthio-2-butanone (compd. No. 516 in Table 1)

30 mp: 100-101 °C

IR(KBr, cm⁻¹): 3340, 1730, 1705, 1683, 1662

NMR(CDCl₃, δ): 0.89(d, J=6.0Hz, 6H), 1.30-1.75(m, 3H), 1.99(s, 3H), 2.85-3.25(m, 4H), 3.75(s, 3H), 4.12(m, 1H), 4.95-5.20(m, 2H), 5.10(s, 2H), 6.54(d, J=7Hz, 1H), 6.78(d, J=8.6Hz, 2H), 7.06(d, J=8.6Hz, 2H), 7.35(s, 5H)

35

Example 199

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-(4-hydroxyphenyl)-1-methylthio-2-butanone (compd. No. 520 in Table 1)

40

mp: 108-111 °C

IR(KBr, cm⁻¹): 3440, 3340, 1725, 1683, 1658

NMR(CDCl₃, δ): 0.89(d, J=5.9Hz, 6H), 1.30-1.75(m, 3H), 1.99(s, 3H), 2.89(m, 1H), 2.99-3.30(m, 3H), 4.14(m, 1H), 4.95-5.10(m, 2H), 5.10(s, 2H), 5.72(s, 1H), 6.58-6.80(m, 1H), 6.70(d, J=8.2Hz, 2H), 6.98(d, J=8.2Hz, 2H), 7.35(s, 5H)

45

Example 200

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -4-(2-thienyl)-2-butanone (compd. No. 527 in Table 1)

50

mp: 93-97 °C

IR(KBr, cm⁻¹): 3340, 3290, 1728, 1688, 1655

NMR(CDCl₃, δ): 0.92(d, J=6.2Hz, 6H), 1.35-1.75(m, 3H), 2.0(s, 3H), 3.14(d, J=15Hz, 1H), 3.23-3.50(m, 3H), 4.18(m, 1H), 4.93-5.13(m, 2H), 5.11(s, 2H), 6.70-6.85(m, 2H), 6.90(m, 1H), 7.14(d, J=5.1Hz, 1H), 7.35(s, 5H)

55

Example 201

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-4-(2-thienyl)-2-butanone (compd. No. 529 in Table 1)

mp: 106-107 °C

5 IR(KBr, cm⁻¹): 3350, 3300, 1730, 1692, 1662

NMR(CDCl₃, δ): 0.92(d, J=6.0Hz, 6H), 1.38-1.75(m, 3H), 3.12-3.43(m, 4H), 3.64(s, 2H), 4.18(m, 1H), 4.90-5.15(m, 2H), 5.11(s, 2H), 6.16(d, J=3.1Hz, 1H), 6.30(m, 1H), 6.67-6.88(m, 2H), 6.89(m, 1H), 7.13(d, J=5.1Hz, 1H), 7.30-7.40(m, 6H)

10 Example 202

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -5-phenyl-2-pentanone (compd. No. 534 in Table 1)

15 mp: 119-120 °C

IR(KBr, cm⁻¹): 3320, 1715, 1685, 1645

NMR(CDCl₃, δ): 0.95(d, J=6.2Hz, 6H), 1.40-1.75(m, 3H), 1.95(m, 1H), 2.05(s, 3H), 2.28(m, 1H), 2.63(t, J=7.8Hz, 2H), 3.17(d, J=15Hz, 1H), 3.33(d, J=15Hz, 1H), 4.18(m, 1H), 4.86(m, 1H), 4.99(d, J=7Hz, 1H), 5.12(s, 2H), 6.58(d, J=7Hz, 1H), 7.10-7.40(m, 10H)

20

Example 203

Preparation of (s)-3-((s)-4-methyl-2-phenoxyacetylaminovaleryl-amino)-1-methylthio-5-phenyl-2-pentanone (compd. No. 536 in Table 1)

25

IR(KBr, cm⁻¹): 3260, 1720, 1650

NMR(CDCl₃, δ): 0.85-1.02(m, 6H), 1.50-1.80(m, 3H), 1.93(m, 1H), 2.06(s, 3H), 2.30(m, 1H), 2.62(t, J=7.6Hz, 2H), 3.17(d, J=14Hz, 1H), 3.32(d, J=14Hz, 1H), 4.50(m, 1H), 4.54(s, 2H), 4.88(m, 1H), 6.63(d, J=7Hz, 1H), 6.82-7.10(m, 4H), 7.10-7.40(m, 7H)

30

Example 204

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-5-phenyl-2-pentanone (compd. No. 540 in Table 1)

35

mp: 73-77 °C

IR(KBr, cm⁻¹): 3340, 1704, 1680, 1658

NMR(CDCl₃, δ): 0.94(d, J=5.9Hz, 6H), 1.40-1.75(m, 3H), 1.91(m, 1H), 2.21(m, 1H), 2.61(t, J=7.5Hz, 2H), 3.15-3.35(m, 2H), 3.70(s, 2H), 4.16(m, 1H), 4.78(m, 1H), 5.02(d, J=7.5Hz, 1H), 5.12(s, 2H), 6.20(d, J=2.9Hz, 1H), 6.28(m, 1H), 6.59(d, J=7Hz, 1H), 7.08-7.45(m, 11H)

40

Example 205

Preparation of (s)-3-((R)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-5-phenyl-2-pentanone (compd. No. 540 in Table 1)

45

mp: 107 °C

IR(KBr, cm⁻¹): 3320, 1725, 1690, 1645

NMR(CDCl₃, δ): 0.95(d, J=6.1Hz, 6H), 1.35-2.0(m, 4H), 2.25(m, 1H), 2.50-2.65(m, 2H), 3.20(d, J=15Hz, 2H), 3.28(d, J=15Hz, 1H), 3.70(s, 2H), 4.17(m, 1H), 4.78(m, 1H), 5.10(m, 1H), 5.12(d, J=1.8Hz, 2H), 6.20(d, J=2.1Hz, 1H), 6.27(m, 1H), 6.63(m, 1H), 7.10-7.40(m, 11H)

50

Example 206

Preparation of (s)-1-furfurylthio-3-((s)-4-methyl -2-phenoxyacetylaminovaleryl-amino)-5-phenyl-2-pentanone (compd. No. 543 in Table 1)

55

IR(KBr, cm⁻¹): 3270, 1720, 1655

NMR(CDCl₃, δ): 0.90-0.95(m, 6H), 1.48-1.80(m, 3H), 1.90(m, 1H), 2.22(m, 1H), 2.60(t, J = 7.8Hz, 2H), 3.22(d, J = 15Hz, 1H), 3.30(d, J = 15Hz, 1H), 3.71(s, 2H), 4.50(m, 1H), 4.54(s, 2H), 4.78(m, 1H), 6.21(m, 1H), 6.28(m, 1H), 6.62(d, J = 8Hz, 1H), 6.86(d, J = 8Hz, 1H), 6.90-6.98(m, 1H), 7.03(t, J = 7.3Hz, 1H), 7.06-7.36(m, 9H)

5 Example 207

Preparation of 3-((s)-2-benzyloxycarbonylamino -4-methylvaleryl-amino)-1-methylthio-4-(1-naphthyl)-2-butanone (compd. No. 547 in Table 1)

10 mp: 77-80 °C

IR(KBr, cm⁻¹): 3340, 1700, 1685, 1665

NMR(CDCl₃, δ): 0.78-0.90(m, 6H), 1.20-1.65(m, 3H), 1.92(s, 1.5H), 1.95(s, 1.5H), 2.93(t, J = 14Hz, 2H), 3.52(d, J = 7.1Hz, 2H), 4.07(m, 1H), 4.92(m, 1H), 5.09(s, 2H), 5.18(m, 1H), 6.55-6.65(m, 1H), 7.20-7.45(m, 7H), 7.50-7.62(m, 2H), 7.76(dd, J = 2.7Hz, 7.8Hz, 1H), 7.86(d, J = 8.0Hz, 1H), 8.20(d, J = 7.8Hz, 1H)

15

Example 208

Preparation of 3-((s)-2-benzyloxycarbonylamino -4-methylvaleryl-amino)-1-furfurylthio-4-(1-naphthyl)-2-butanone (compd. No. 550 in Table 1)

20 mp: 71-74 °C

IR(KBr, cm⁻¹): 3330, 1730, 1690, 1650

NMR(CDCl₃, δ): 0.78-0.90(m, 6H), 1.25-1.60(m, 3H), 2.90-3.05(m, 2H), 3.49(d, J = 7.1Hz, 2H), 3.57(d, J = 6.3Hz, 2H), 4.08(m, 1H), 4.88(m, 1H), 5.08(s, 2H), 5.11(m, 1H), 6.12(m, 1H), 6.25(m, 1H), 6.57(d, J = 7Hz, 0.5H), 6.66(d, J = 7Hz, 0.5H), 7.20-7.40(m, 8H), 7.42-7.62(m, 2H), 7.75(dd, J = 3.1Hz, 8.2Hz, 1H), 7.85(d, J = 8.0Hz, 1H), 8.17(d, J = 8.0Hz, 1H)

25

Example 209

Preparation of 1-furfurylthio-3-((s)-4-methyl-2-phenoxyacetyl-aminovaleryl-amino)-4-(1-naphthyl)-2-butanone (compd. No. 555 in Table 1)

30

IR(KBr, cm⁻¹): 3280, 1650

NMR(CDCl₃, δ): 0.72-0.92(m, 6H), 1.20-1.70(m, 3H), 2.90-3.05(m, 2H), 3.40-3.60(m, 2H), 3.60(s, 2H), 4.41(m, 1H), 4.45(s, 2H), 5.11(m, 1H), 6.14(m, 1H), 6.25(m, 1H), 6.65-7.12(m, 5H), 7.20-7.42(m, 5H), 7.42-7.65(m, 2H), 7.70-7.90(m, 2H), 8.13(t, J = 8.3Hz, 1H)

35

Example 210

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio -4-(2-naphthyl)-2-butanone (compd. No. 559 in Table 1)

40

mp: 101-103 °C

IR(KBr, cm⁻¹): 3340, 1730, 1690, 1650

NMR(CDCl₃, δ): 0.65-0.76(m, 2.4H), 0.83(d, J = 5.7Hz, 3.6H), 1.25-1.63(m, 3H), 1.97(s, 1.8H), 1.99(s, 1.2H), 3.05-3.40(m, 4H), 4.08(m, 1H), 4.94-5.07(m, 3H), 5.16(q, J = 7.0Hz, 1H), 6.52(d, J = 7Hz, 0.4H), 6.68(d, J = 7Hz, 0.6H), 7.25-7.40(m, 6H), 7.40-7.50(m, 2H), 7.60(s, 1H), 7.70-7.85(m, 3H)

45

Example 211

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-furfurylthio-4-(2-naphthyl)-2-butanone (compd. No. 563 in Table 1)

50

mp: 103-104 °C

IR(KBr, cm⁻¹): 3330, 3300, 1710, 1690, 1650

NMR(CDCl₃, δ): 0.70-0.80(m, 1.8H), 0.84(d, J = 5.7Hz, 4.2H), 1.20-1.60(m, 3H), 3.10-3.40(m, 4H), 3.61(s, 1.4H), 3.64(s, 0.6H), 4.10(m, 1H), 4.90-5.15(m, 4H), 6.14(m, 1H), 6.26(m, 1H), 6.52(d, J = 7Hz, 0.3H), 6.64(d, J = 7Hz, 0.7H), 7.26-7.40(m, 7H), 7.40-7.50(m, 2H), 7.59(m, 1H), 7.76-7.84(m, 3H)

55

Example 212

Preparation of (s)-1-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-3-methylthio-1-phenyl-2-propanone (compd. No. 565 in Table 1)

5

IR(neat, cm^{-1}): 3330, 1710, 1650

NMR(CDCl_3 , δ): 0.80-1.0(m, 6H), 1.20-1.75(m, 3H), 2.00(s, 3H), 3.08(dd, $J=3.4\text{Hz}$, 14Hz, 1H), 3.25(dd, $J=3.8\text{Hz}$, 14Hz, 1H), 4.25(m, 1H), 5.09(s, 1H), 5.13(s, 1H), 5.92(d, $J=6.3\text{Hz}$, 1H), 7.17(m, 1H), 7.25-7.45(m, 10H)

10

Example 213

Preparation of (s)-4-benzyloxy-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1-methylthio-2-butanone (compd. No. 571 in Table 1)

15

mp: 58-70 °C

IR(KBr, cm^{-1}): 3340, 1723, 1688, 1650

NMR(CDCl_3 , δ): 0.85-1.05(m, 6H), 1.40-1.80(m, 3H), 2.02(s, 3H), 3.22(d, $J=15\text{Hz}$, 1H), 3.35(d, $J=15\text{Hz}$, 1H), 3.65(m, 1H), 3.93(m, 1H), 4.23(m, 1H), 4.43(d, $J=13\text{Hz}$, 1H), 4.53(d, $J=13\text{Hz}$, 1H), 5.0(m, 1H), 5.11(s, 2H), 5.15(m, 1H), 6.90(m, 1H), 7.20-7.45(m, 10H)

20

Example 214

Preparation of (s)-3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-1,5-bis(methylthio)-2-pentanone (compd. No. 584 in Table 1)

25

mp: 61-67 °C

IR(KBr, cm^{-1}): 3320, 1715, 1682, 1642

NMR(CDCl_3 , δ): 0.93(d, $J=5.4\text{Hz}$, 6H), 1.45-2.35(m, 5H), 2.06(s, 3H), 2.07(s, 3H), 2.49(t, $J=6.9\text{Hz}$, 2H), 3.24(d, $J=14\text{Hz}$, 1H), 3.36(d, $J=14\text{Hz}$, 1H), 4.23(m, 1H), 4.93(m, 1H), 5.11(s, 2H), 5.35(m, 1H), 6.98(m, 1H), 7.34(s, 5H)

30

Example 215

Preparation of 3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-5-furfurylthio-1-methylthio-2-pentanone (compd. No. 588 in Table 1)

35

IR(neat, cm^{-1}): 3350, 3310, 1715, 1690, 1660, 1643

NMR(CDCl_3 , δ): 0.93(d, $J=5.5\text{Hz}$, 3H), 0.95(d, $J=5.5\text{Hz}$, 3H), 1.45-1.93(m, 4H), 2.05(s, 3H), 2.13(m, 1H), 2.50(t, $J=6.7\text{Hz}$, 2H), 3.14-3.42(m, 2H), 3.70(s, 2H), 4.21(m, 1H), 4.89(m, 1H), 5.12(s, 2H), 5.13(m, 1H), 6.19(d, $J=2.9\text{Hz}$, 1H), 6.32(m, 1H), 6.77(m, 1H), 7.30-7.40(m, 5H)

40

Example 216

Preparation of (s)-4-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-6-furfurylthio -5-oxohexanoic acid methyl ester (compd. No. 598 in Table 1)

45

IR(neat, cm^{-1}): 3330, 1735, 1715, 1660

NMR(CDCl_3 , δ): 0.93(d, $J=5.9\text{Hz}$, 6H), 1.42-2.50(m, 7H), 3.29(d, $J=15\text{Hz}$, 1H), 3.36(d, $J=15\text{Hz}$, 1H), 3.65(s, 3H), 3.70(s, 2H), 4.19(m, 1H), 4.77(m, 1H), 5.11(s, 2H), 5.16(m, 1H), 6.22(d, $J=2.4\text{Hz}$, 1H), 6.28(m, 1H), 6.90(m, 1H), 7.25-7.40(m, 6H)

50

Example 217

Preparation of (s)-4-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-6-furfurylthio -5-oxohexanoic acid (compd. No. 600 in Table 1)

55

IR(neat, cm^{-1}): 3420, 1710, 1650

NMR(CDCl_3 , δ): 0.91(d, $J=5.0\text{Hz}$, 6H), 1.40-2.75(m, 7H), 3.31(s, 2H), 3.68(s, 2H), 4.22(m, 1H), 4.78(m, 1H),

5.09(s, 2H), 5.43(m, 1H), 6.19(d, J = 2.1Hz, 1H), 6.26(m, 1H), 6.91(m, 1H), 7.13-7.35(m, 7H)

Example 218

- 5 Preparation of 1-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-3-furfurylthio-1-propoxy-2-propanone (compd. No. 604 in Table 1)

IR(neat, cm^{-1}): 3300, 1710, 1660

- 10 NMR(CDCl_3 , δ): 0.89(t, J = 7.5Hz, 3H), 0.95(d, J = 5.9Hz, 6H), 1.40-1.80(m, 5H), 3.37(d, J = 15Hz, 1H), 3.50(d, J = 15Hz, 1H), 3.50-3.67(m, 2H), 3.68(s, 2H), 4.25(m, 1H), 5.12(s, 2H), 5.14(m, 1H), 5.76(m, 1H), 6.20(d, J = 2.5Hz, 1H), 6.28(m, 1H), 6.88(d, J = 9Hz, 0.7H), 6.97(d, J = 9Hz, 0.3H), 7.30-7.40(m, 6H)

Example 219

- 15 Preparation of 3-((s)-2-benzyloxycarbonylamino-4-methylvaleryl-amino)-4-phenyl-1-phenylthio-3-buten-2-one (compd. No. 610 in Table 1)

mp: 142-143 °C

IR(KBr, cm^{-1}): 3385, 1692, 1650

- 20 NMR(CDCl_3 , δ): 0.93(d, J = 5.2Hz, 3H), 0.96(d, J = 6.1Hz, 3H), 1.52(m, 1H), 1.70(m, 2H), 3.98(s, 2H), 4.38(m, 1H), 5.05(d, J = 6.5Hz, 1H), 5.13(s, 2H), 7.09(s, 1H), 7.20-7.48(m, 15H), 7.88(s, 1H)

Example 220

- 25 Preparation of (s)-1-furfurylthio-3-[(s)-2-{3-(2-furyl)acryloylamino}-4-methylvaleryl-amino]-2-heptane (compd. No. 645 in Table 1)

IR(KBr, cm^{-1}): 3272, 1715, 1651, 1618

- 30 NMR(CDCl_3 , δ): 0.81(t, J = 6.7Hz, 3H), 0.92(d, J = 5.6Hz, 6H), 1.13-1.41(m, 4H), 1.45-1.79(m, 4H), 1.85(m, 1H), 3.27(d, J = 15Hz, 1H), 3.36(d, J = 15Hz, 1H), 3.72(s, 2H), 4.62-4.83(m, 2H), 6.18-6.60(m, 6H), 7.06(d, J = 7.7Hz, 1H), 7.28-7.51(m, 3H)

Example 221

- 35 Preparation of (s)-3-((s)-1-benzyloxycarbonyl-2-pyrrolidinyl-amino)-1-furfurylthio-2-heptanone (compd. No. 669 in Table 1)

IR(neat, cm^{-1}): 3320, 1720, 1680

- 40 NMR(CDCl_3 , δ): 0.86(t, J = 6.7Hz, 3H), 1.10-1.39(m, 4H), 1.55(m, 1H), 1.75-2.10(m, 4H), 2.21(m, 1H), 3.03-3.38(m, 2H), 3.38-3.63(m, 2H), 3.63-3.78(m, 2H), 4.36(m, 1H), 4.67(m, 1H), 5.18(s, 2H), 6.22(m, 1H), 6.29(m, 1H), 6.58(m, 1H), 7.22-7.45(m, 6H)

Example 222

- 45 Preparation of (s)-3-((s)-1-benzyloxycarbonyl-2-pyrrolidinyl-carbonylamino)-1-methylthio-4-phenyl-2-butanone (compd. No. 673 in Table 1)

IR(neat, cm^{-1}): 3330, 1705, 1680

- 50 NMR(CDCl_3 , δ): 1.40-2.05(m, 4H), 1.97(s, 3H), 2.85-3.60(m, 6H), 4.31(m, 1H), 5.02(m, 1H), 5.15(s, 2H), 7.12-(d, J = 7.5Hz, 2H), 7.15-7.45(m, 8H)

Example 223

- 55 Preparation of (s)-3-((s)-2-benzyloxycarbonyl-3-perhydroisoquinolyl-carbonylamino)-1-furfurylthio-4-phenyl-2-butanone (compd. No. 683 in Table 1)

IR(neat, cm^{-1}): 3350, 1690

NMR(CDCl_3 , δ): 1.15-1.90(m, 12H), 2.80-3.25(m, 6H), 3.60-3.70(m, 2H), 4.70-5.25(m, 4H), 6.20(m, 1H), 6.29-

(m, 1H), 6.52(m, 1H), 7.0-7.45(m, 11H)

Example 224

- 5 Preparation of (s)-3-[(s)-2-((s)-2-cyclohexylmethoxycarbonylamino-4-methylvalerylamino)-4-methylvalerylamino]-1-furfurylthio-2-heptanone(compd. No. 699 in Table 2)

IR(neat, cm^{-1}): 3300, 1700, 1670, 1640

NMR(CDCl_3 , δ): 0.85-1.70(m, 15H), 1.15-2.0(m, 23H), 3.26(d, J = 15Hz, 1H), 3.32(d, J = 15Hz, 1H), 3.71(s, 2H), 3.87(d, J = 6.4Hz, 2H), 4.12(m, 1H), 4.42(m, 1H), 4.69(m, 1H), 5.03(d, J = 5.8Hz, 1H), 6.22(d, J = 3.3Hz, 1H), 6.28(dd, J = 3.3Hz, 2.1Hz, 1H), 6.47(d, J = 7.5Hz, 1H), 6.76(m, 1H), 7.35(d, J = 2.1Hz, 1H)

Reference Example 3

- 15 Preparation of (s)-1-((s)-2-benzyloxycarbonylamino-4-methylvaleryl)-2-furfurylthioacetylpyrrolidine

IR(neat, cm^{-1}): 3300, 1710, 1640

NMR(CDCl_3 , δ): 0.93(d, J = 5.9Hz, 3H), 0.98(d, J = 6.5Hz, 3H), 1.48(dd, J = 6.9Hz, 6.9Hz, 2H), 1.64-1.80(m, 2H), 1.84-2.28(m, 3H), 3.30(d, J = 15Hz, 1H), 3.42(d, J = 15Hz, 1H), 3.59(m, 1H), 3.70(s, 2H), 3.82(m, 1H), 4.57(m, 1H), 4.74(dd, J = 7.9Hz, 5.9Hz, 1H), 5.03-5.12(m, 2H), 5.39(d, J = 6.8Hz, 1H), 6.23(m, 1H), 6.29(m, 1H), 7.24-7.39(m, 6H)

The following experiments were conducted to evaluate the biological activity of compound (I) prepared in the above Examples.

25 Experiment 1

Assay of Thiol Protease Inhibitory Activity

Inhibitory activity against papain (P-3125, Sigma) and cathepsin B (C-6286, Sigma) was assayed according to the method described in a literature [Biochemical Journal, 201, 189 (1982)]. Cathepsin L was purified from rat kidney according to the method in a literature [Journal of Biochemistry, 100, 35 (1986)], and the inhibitory activity against it was assayed in the same manner as described in the above literature for cathepsin B. Furthermore, m-calpain was purified from rat brain according to a known method [Journal of Biological Chemistry, 254, p.3210 (1984)] and the inhibitory activity against it was assayed by a method described in a literature [Journal of Biological Chemistry, 259, 12489 (1984)]. The results are shown in Tables 3 and 4. It is evident from Tables 3 and 4 that the compounds of the present invention have a potent inhibitory activity against thiol proteases such as papain, cathepsin B, cathepsin L or m-calpain.

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Table 3 (Inhibitory activity against thiol protease)

Compd. of Ex. No. (Compd. No. in Table 1)	I C ₅₀ (μM)			
	papain	cathepsin B	cathepsin L	m-calpain
3 (No. 82)	0.26	0.71	0.016	3.3
4 (No. 83)	0.21	0.044	0.045	12
21 (No. 46)	0.13	0.14	—	4.7
22 (No. 48)	1.1	0.98	1.3	11
23 (No. 49)	2.2	3.7	1.1	6.4
28 (No. 59)	3.4	2.1	1.5	11
30 (No. 66)	0.15	0.59	—	5.1
31 (No. 69)	1.4	0.55	0.63	2.2
33 (No. 76)	0.70	1.2	0.27	6.4
34 (No. 79)	0.36	0.41	0.51	5.5
35 (No. 81)	0.21	0.70	1.1	8.6
36 (No. 85)	2.6	4.9	1.3	2.5
37 (No. 86)	1.3	0.70	0.45	1.5
38 (No. 87)	0.42	0.62	0.72	5.0
39 (No. 88)	0.25	0.29	—	2.2
40 (No. 90)	2.1	0.27	0.85	8.4
41 (No. 91)	2.1	5.7	1.1	1.4
42 (No. 92)	4.5	1.9	0.74	2.3
43 (No. 94)	0.37	0.057	0.038	5.8
44 (No. 96)	0.88	0.17	0.060	2.2
45 (No. 97)	0.51	0.38	0.19	1.1
46 (No. 100)	0.39	0.40	0.10	1.6
49 (No. 107)	0.040	0.59	0.67	1.1
52 (No. 114)	0.34	0.82	—	2.5
53 (No. 115)	9.2	1.1	1.5	6.2
54 (No. 116)	0.38	0.88	0.25	1.4
82 (No. 162)	3.4	2.7	0.32	2.0
83 (No. 161)	4.7	5.0	0.40	1.2

Table 3 (Inhibitory activity against m-calpain) (continued)

Compd. of Ex. No. (Compd.No. in Table 1)	I C ₅₀ (μM)			
	papain	cathepsin B	cathepsin L	m-calpain
91 (No.180)	0.16	0.050	0.069	14
94 (No.188)	0.77	1.1	0.024	9.2
109 (No.238)	4.2	1.1	1.2	13
110 (No.240)	21	3.3	0.98	6.0
120 (No.256)	56	3.9	0.49	26
135 (No.288)	59	0.31	0.054	3.2
150 (No.313)	91	1.1	0.27	5.4
159 (No.333)	0.38	0.75	1.1	1.9
160 (No.334)	35	3.3	6.6	28
162 (No.345)	0.95	5.3	—	3.7
164 (No.348)	35	64	3.2	1.7
165 (No.349)	9.2	7.0	1.9	13
167 (No.354)	>100	30	1.4	20
170 (No.364)	9.2	6.5	8.6	19
174 (No.382)	12	23	1.6	16
190 (No.465)	40	1.6	2.8	7.3
191 (No.479)	>100	3.5	9.3	24
197 (No.511)	13	6.0	1.7	7.8
202 (No.534)	>100	0.25	0.39	13
203 (No.536)	4.4	0.34	0.38	9.1
206 (No.543)	6.0	0.82	0.62	15
209 (No.555)	9.0	6.5	1.5	19
217 (No.600)	26	2.5	11	19

Table 4 (Inhibitory activity against m-calpain)

5	Compd. of Ex. No.	I C ₅₀ (μM)	10	Compd. of Ex. No.	I C ₅₀ (μM)
	(Compd.No. in Table 1)	m-calpain		(Compd. No. in Table 1)	m-calpain
	2 6 (No. 5 7)	2. 8		6 7 (No. 1 3 2)	2. 1
	2 9 (No. 6 5)	3. 6		6 8 (No. 1 3 5)	2. 1
10	3 2 (No. 7 3)	6. 2		6 9 (No. 1 4 0)	5. 0
	4 7 (No. 1 0 2)	1. 3		7 1 (No. 1 4 2)	4. 2
	4 8 (No. 1 0 4)	1. 0		7 7 (No. 1 5 1)	1. 2
15	5 5 (No. 1 1 7)	1. 5		7 8 (No. 1 0 3)	6. 0
	5 6 (No. 1 1 8)	5. 2		7 9 (No. 1 5 3)	1. 9
	5 7 (No. 1 1 9)	5. 3		8 0 (No. 1 5 5)	4. 2
20	5 8 (No. 1 2 0)	1. 6		8 1 (No. 1 5 7)	3. 4
	5 9 (No. 1 2 1)	4. 2		8 4 (No. 1 6 5)	2. 1
	6 0 (No. 1 2 2)	1. 3		8 5 (No. 1 6 6)	1. 3
25	6 1 (No. 1 2 3)	1. 9		9 3 (No. 1 8 2)	7. 8
	6 2 (No. 1 2 4)	4. 3		1 0 5 (No. 2 2 6)	1. 3
	6 3 (No. 1 2 5)	5. 5		1 0 6 (No. 2 2 8)	3. 1
30	6 4 (No. 1 2 6)	4. 3		1 0 7 (No. 2 3 0)	4. 2
	6 5 (No. 1 2 8)	5. 0		1 3 9 (No. 2 9 7)	4. 5
35	6 6 (No. 1 3 0)	1. 4		1 8 3 (No. 4 2 3)	9. 6
				compd. of Ref. Ex. No. 3	> 1 0 0

Experiment 2

Confirmation of reversible inhibitory

According to the assay for inhibitory activity against calpain in Experiment 1, reversible inhibitory activity of the present compounds was confirmed as follows.

To an imidazole buffer (54 μl) were added 500mM CaCl₂ solution (1 μl), 5mM solution of the synthetic substrate described in the literature (4 μl), 10 μM -150 μM inhibitor solution (1 μl) and m-calpain solution (40 μl), and the mixture was incubated for 0 to 20 minutes at a temperature of 10°C. Then, 100mM EDTA solution (5 μl) was added to inactivate the enzymatic activity. To the mixture was then added imidazole buffer (900 μl) followed by an addition of 5mM synthetic substrate solution (40 μl) and 500mM CaCl₂ solution (10 μl), and the decomposition rate of the synthetic substrate was measured for 10 minutes at a temperature of 30°C to determine the remaining activity of the enzyme.

The compounds of Examples 3, 113 and 190 were used as the inhibitor, and E-64 which is an irreversible inhibitor was also used for comparison. The results are shown in Figs. 1 to 3. As is clear from Figs. 1 to 3, enzymatic activity rapidly disappeared in proportion to the incubation period when used irreversible inhibitor E-64, while the activity nearly equal to that of a control remained when used the compounds of the present invention, indicating that the present compounds are a reversible inhibitor.

Experiment 3Acute toxicity

- 5 A suspension of the present compound in 0.5% CMC-Na aqueous solution was orally administered to SD female and male rats, and the rats were observed for 7 days. The LD₅₀ value of the compound prepared in Example 94 was: > 2,000 mg/kg.

The following formulation examples are illustrative only.

10 Formulation 1(1) Tablet

- 15 The following ingredients were admixed in a conventional manner and compressed on a customary tablet machine.

20	Compound in Example 94	30 mg
	Crystalline cellulose	60 mg
	Corn starch	100 mg
	Lactose	200 mg
	Magnesium stearate	4 mg

25 (2) Soft gelatin capsule

The following ingredients were admixed in a conventional manner and filled in soft capsules.

30	Compound in Example 94	30 mg
	Olive oil	300 mg
	Lecithin	20 mg

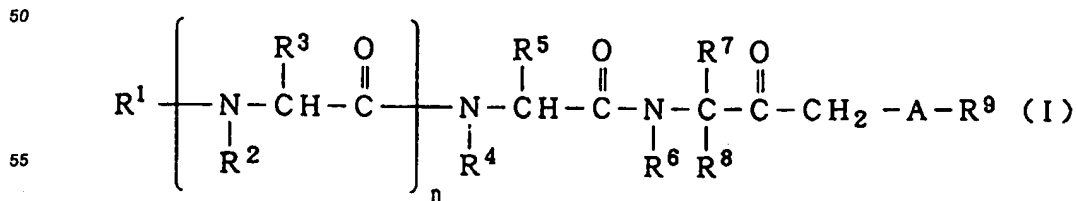
35 (3) Injection

The following ingredients were admixed in a conventional manner and filled in an ampoule in a volume of 1 ml.

40	Compound in Example 106	2.5 mg
	Sodium chloride	3.5 mg
	Distilled water for injection	1 ml

45 **Claims**

1. A ketone derivative of the general formula (I):



wherein R¹ is hydrogen atom, R¹⁰-CO-, R¹⁰-O-CO-, R¹⁰-SO₂- or R¹⁰-NH-CO- (in which R¹⁰ is C₁ - C₂₀ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, C₃ - C₁₅ cycloalkenyl group, optionally substituted C₆ - C₁₄ aryl group, optionally substituted and partially hydrogenated C₁₀ - C₁₄ aryl group, fluorenyl group, optionally substituted heterocyclic group, C₃ - C₁₅ cycloalkyloxy group, optionally substituted C₆ - C₁₄ aryloxy group, optionally substituted and partially hydrogenated C₆ - C₁₄ aryloxy group, optionally substituted heterocyclic oxy group, optionally substituted C₇ - C₂₀ aralkyloxy group and optionally substituted C₆ - C₁₄ arylthio group; C₃ - C₁₅ cycloalkyl group; optionally substituted C₆ - C₁₄ aryl group; optionally substituted and partially hydrogenated C₆ - C₁₄ aryl group; optionally substituted C₂ - C₁₀ alkenyl group; or optionally substituted heterocyclic group);

R², R⁴ and R⁶ each are independently hydrogen atom or C₁ - C₅ alkyl group;

R³ and R⁵ each are independently hydrogen atom, C₇ - C₂₀ aralkyloxy group, optionally substituted C₆ - C₁₄ aryl group, C₁ - C₁₀ alkoxy group or optionally substituted C₁ - C₂₀ alkyl group; or

R² and R³ and/or R⁴ and R⁵ taken together may form an optionally substituted nitrogen-containing heterocyclic ring;

R⁷ is C₁ - C₂₀ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, hydroxyl group, C₁ - C₅ alkoxy group optionally substituted by heterocyclic group, C₆ - C₁₄ aryloxy group, C₇ - C₂₀ aralkyloxy group, C₁ - C₅ alkylthio group optionally substituted by heterocyclic group, C₆ - C₁₄ arylthio group, C₇ - C₂₀ aralkylthio group, carboxyl group, carbamoyl group, C₂ - C₆ alkoxycarbonyl group, heterocyclic group and optionally substituted C₆ - C₁₄ aryl group; hydrogen atom; C₇ - C₂₀ aralkyloxy group; optionally substituted C₆ - C₁₄ aryl group or C₁ - C₁₀ alkoxy group;

R⁸ is hydrogen atom, C₁ - C₅ alkyl group or optionally substituted C₇ - C₂₀ aralkyl group; or

R⁷ and R⁸ taken together may form optionally substituted benzylidene group or C₃ - C₁₅ cycloalkyl group;

A is -S-, -SO-, -SO₂-, -O- or -N(R¹¹)- (in which R¹¹ is hydrogen atom or optionally substituted C₁ - C₂₀ alkyl group), and

(1) when A is -S-, -SO- or -SO₂-, then R⁹ is optionally substituted C₆ - C₁₄ aryl group or -(CH₂)_m-X (in which X is hydrogen atom, hydroxyl group, C₁ - C₅ alkylthio group, C₂ - C₆ alkoxycarbonylamino group, optionally substituted heterocyclic group, amino group, C₁ - C₅ monoalkylamino group, C₂ - C₁₀ dialkylamino group, C₂ - C₆ acylamino group, halogen atom, C₁ - C₅ alkoxy group, optionally substituted C₆ - C₁₄ aryl group or optionally substituted C₆ - C₁₄ aryloxy group; and m is 0 or an integer of 1 to 15); provided that if R¹ is benzyloxycarbonyl group, R⁴, R⁶ and R⁸ all are hydrogen atom, R⁵ is benzyl group, R⁷ is methyl group and n is 0, then -A-R⁹ is not methylthio group;

(2) when A is -O-, then R⁹ is hydrogen atom or -(CH₂)₁-X (in which 1 is an integer of 1 to 15; and X is as defined above); or

(3) when A is -N(R¹¹)-, then R⁹ is optionally substituted C₆ - C₁₄ aryl group or -(CH₂)_m-X (in which X and m are as defined above); or R⁹ and R¹¹ taken together may form an optionally substituted nitrogen-containing heterocyclic ring; and

n is 0 or 1, or pharmaceutically acceptable salts thereof.

2. The compound according to Claim 1 wherein A is -S-, -SO-, -SO₂- or -N(R¹¹)- (in which R¹¹ is optionally substituted C₁ - C₁₅ alkyl group).

3. The compound according to Claim 2 wherein R⁹ is -(CH₂)_m-X (in which X is hydroxyl group, C₁ - C₅ alkylthio group, C₂ - C₆ alkoxycarbonylamino group, optionally substituted heterocyclic group, amino group, C₁ - C₅ monoalkylamino group, C₂ - C₁₀ dialkylamino group, C₂ - C₆ acylamino group, halogen atom, C₁ - C₅ alkoxy group, optionally substituted C₆ - C₁₄ aryl group or optionally substituted C₆ - C₁₄ aryloxy group; and m is an integer of 1 to 10).

4. The compounds according to Claim 3 wherein R¹ is hydrogen atom, R¹⁰-CO-, R¹⁰-O-CO-, R¹⁰-SO₂- or R¹⁰-NH-CO- (in which R¹⁰ is C₁ - C₁₅ alkyl group optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, C₃ - C₁₅ cycloalkenyl group, optionally substituted C₆ - C₁₄ aryl group, optionally substituted and partially hydrogenated C₁₀ - C₁₄ aryl group, optionally substituted heterocyclic group, C₃ - C₁₅ cycloalkyloxy group, optionally substituted C₆ - C₁₄ aryloxy group, optionally substituted and partially hydrogenated C₆ - C₁₄ aryloxy group, optionally substituted heterocyclic oxy group, optionally substituted C₇ - C₂₀ aralkyloxy group and optionally substituted C₆ - C₁₄ arylthio group; C₃ - C₁₅ cycloalkyl group; optionally substituted C₆ - C₁₄ aryl

group; optionally substituted and partially hydrogenated C₆ - C₁₄ aryl group; optionally substituted C₂ - C₁₀ alkenyl group; or optionally substituted heterocyclic group); R⁴ and R⁶ each is independently hydrogen atom or C₁ - C₅ alkyl group; R⁵ is hydrogen atom, optionally substituted C₆ - C₁₄ aryl group, C₁ - C₁₀ alkoxy group or optionally substituted C₁ - C₁₅ alkyl group; R⁷ is C₁ - C₁₅ alkyl group
 5 optionally substituted by one or more substituents selected from the group consisting of C₃ - C₁₅ cycloalkyl group, hydroxyl group, C₁ - C₅ alkoxy group optionally substituted by heterocyclic group, C₆ - C₁₄ aryloxy group, C₇ - C₂₀ aralkyloxy group, C₁ - C₅ alkylthio group optionally substituted by heterocyclic group, C₆ - C₁₄ arylthio group, C₇ - C₂₀ aralkylthio group, carboxyl group, carbamoyl group, C₂ - C₆ alkoxycarbonyl group and heterocyclic group; hydrogen atom; optionally substituted C₆
 10 - C₁₄ aryl group or C₁ - C₁₀ alkoxy group; R⁸ is hydrogen atom.

5. The compound according to Claim 4 wherein A is -S- or -N(R¹¹)- (in which R¹¹ is as defined in Claim 2) and n is 0.
- 15 6. The compound according to Claim 5 wherein R¹ is R¹⁰-CO- or R¹⁰-O-CO- (in which R¹⁰ is as defined in Claim 4).
7. The compound according to Claim 6 wherein R⁹ is -(CH₂)_m-X (in which X is optionally substituted heterocyclic group).
- 20 8. A pharmaceutical composition which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
9. A pharmaceutical composition for treating a disease caused by hypersthenia of thiol protease, which
 25 comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
10. A pharmaceutical composition for treating a disease due to the collapse of skeletal muscle, which
 30 comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
11. The pharmaceutical composition according to Claim 10, wherein the disease due to the collapse of skeletal muscle is muscular dystrophy.
- 35 12. The pharmaceutical composition according to Claim 10, wherein the disease due to the collapse of skeletal muscle is amyotrophy.
13. A pharmaceutical composition for treating ischemic disease, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 40 14. The pharmaceutical composition according to Claim 13, wherein the ischemic disease is cardiac infarction.
15. The pharmaceutical composition according to Claim 13, wherein the ischemic disease is stroke.
- 45 16. A pharmaceutical composition for treating conscious disturbance or motor disturbance caused by brain trauma, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 50 17. A pharmaceutical composition for treating a disease caused by demyelination of neurocyte, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
18. The pharmaceutical composition according to Claim 17, wherein the disease caused by demyelination
 55 of neurocyte is multiple sclerosis.
19. The pharmaceutical composition according to Claim 17, wherein the disease caused by demyelination of neurocyte is neuropathy of peripheral nerve.

20. A pharmaceutical composition for treating cataract, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 5 21. A pharmaceutical composition for treating inflammation, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
22. A pharmaceutical composition for treating allergic disease, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 10 23. A pharmaceutical composition for treating hepatic disease, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
24. The pharmaceutical composition according to Claim 23, wherein said hepatic disease is fulminant hepatitis.
- 15 25. A pharmaceutical composition for treating osteoporosis, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 20 26. A pharmaceutical composition for treating hypercalcemia, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
27. A pharmaceutical composition for treating a disease caused by abnormal activation of sex hormone receptors, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 25 28. The pharmaceutical composition according to Claim 27, wherein said disease caused by abnormal activation of sex hormone receptors is breast carcinoma.
29. The pharmaceutical composition according to Claim 27, wherein said disease caused by abnormal activation of sex hormone receptors is prostatic carcinoma.
- 30 30. The pharmaceutical composition according to Claim 27, wherein said disease caused by abnormal activation of sex hormone receptors is prostatomegaly.
- 35 31. A pharmaceutical composition for inhibiting the growth of tumor cells or for preventing metastasis of tumor, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.
- 40 32. A pharmaceutical composition for inhibiting platelet-aggregation, which comprises, as an active ingredient, a compound of Claim 1 together with pharmaceutically acceptable carriers.

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Fig. 1

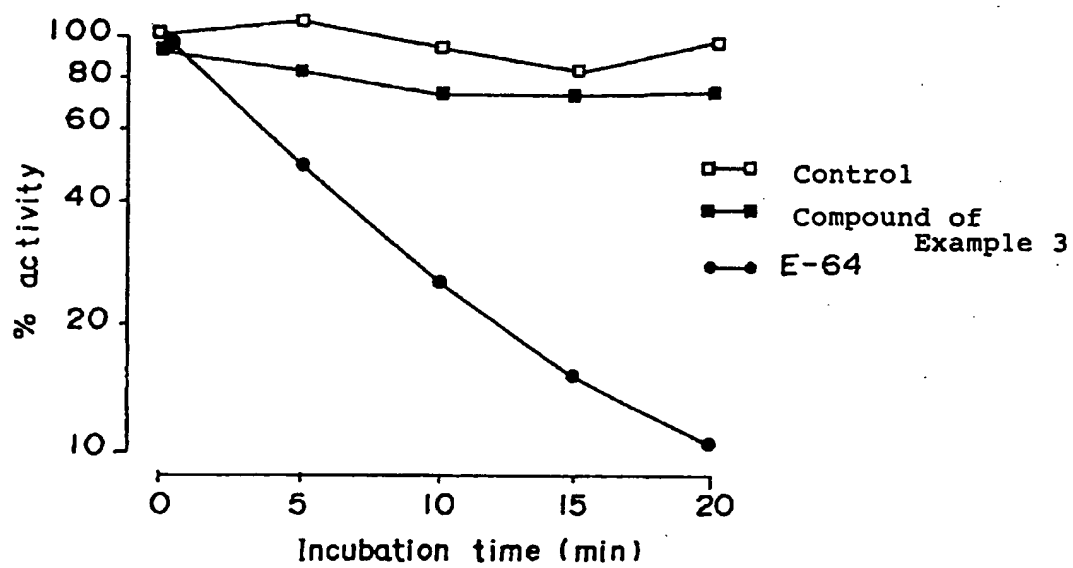


Fig. 2

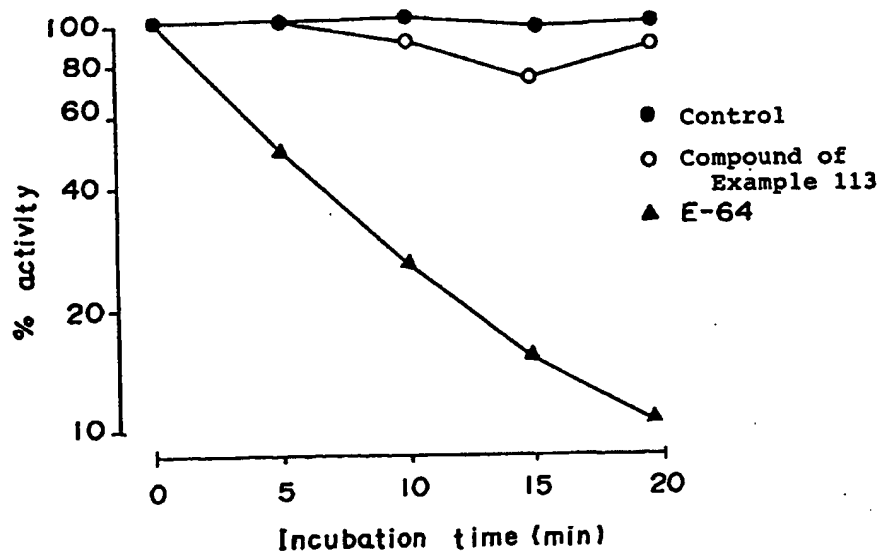
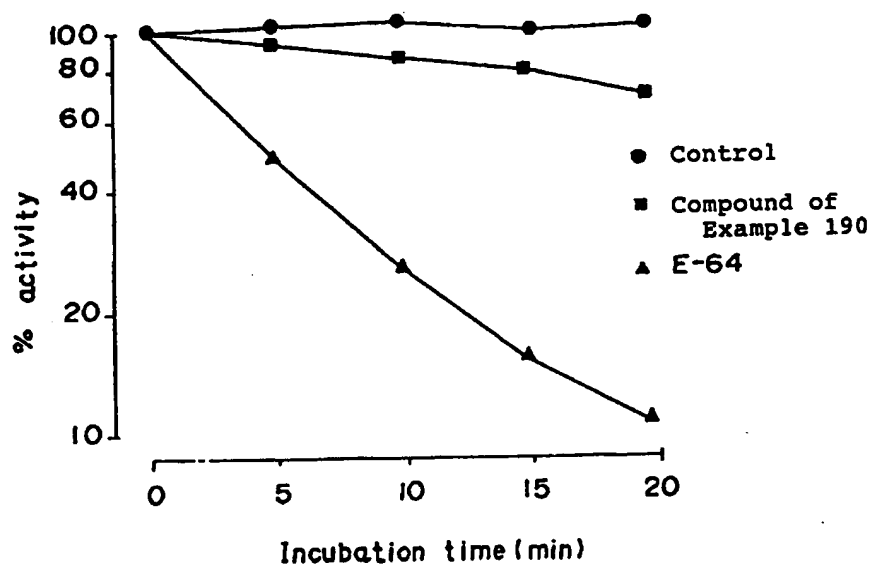


Fig. 3



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Application Number

EP 92 11 1129

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	JOURNAL OF BIOLOGICAL CHEMISTRY vol. 263, no. 6, 25 February 1988, BALTIMORE, MD US pages 2768 - 2772 E. SHAW 'Peptidyl Sulfonium Salts. A NEW CLASS OF PROTEASE INHIBITORS' * the whole document, and in particular RN [114317-27-0], RN [114317-35-0] *	1,2	C07D307/56 C07D307/84 C07D307/85 C07D307/68 C07D307/38 C07D307/42 C07D307/52 C07D213/32
Y	---	1,2,8-32	C07D235/06 C07D261/08
Y	EP-A-0 272 671 (SYNTEX INC.) * page 2, line 1 - page 3, line 4; claims 1,39-47 *	1,2,8-32	C07D263/20 C07D277/26 C07D295/125 C07D405/12
A	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY. vol. 110, no. 13, 1988, GASTON, PA US pages 4429 - 4431 R. A. SMITH ET AL. 'New Inhibitors of Cysteine Proteinases. Peptidyl Acyloxymethyl Ketones and the Quiescent Nucleofuge Strategy' * the whole document *	1	C07D407/12 C07D409/12 C07C271/54 C07C317/28 C07C323/41 C07K5/06

D,A	BIOCHEMISTRY. vol. 30, no. 19, 1991, EASTON, PA US pages 4678 - 4687 A. KRANTZ ET AL. 'Peptidyl (Acyloxy)methyl Ketones and the Quiescent Affinity Label Concept: The Departing Group as a Variable Structural Element in the Design of Inactivators of Cysteine Proteinases' * the whole document *	1	C07D C07K C07C

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The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 08 OCTOBER 1992	Examiner PAISDOR B.
<div style="display: flex; justify-content: space-between;"> <div> <p style="margin: 0;">CATEGORY OF CITED DOCUMENTS</p> <p style="margin: 0;">X : particularly relevant if taken alone</p> <p style="margin: 0;">Y : particularly relevant if combined with another document of the same category</p> <p style="margin: 0;">A : technological background</p> <p style="margin: 0;">O : non-written disclosure</p> <p style="margin: 0;">P : intermediate document</p> </div> <div> <p style="margin: 0;">T : theory or principle underlying the invention</p> <p style="margin: 0;">E : earlier patent document, but published on, or after the filing date</p> <p style="margin: 0;">D : document cited in the application</p> <p style="margin: 0;">L : document cited for other reasons</p> <p style="margin: 0;">A : member of the same patent family, corresponding document</p> </div> </div>			



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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
P,X	CHEMICAL ABSTRACTS, vol. 117, no. 3, 20 July 1992, Columbus, Ohio, US; abstract no. 22302m, J. V. ROBINSON ET AL. 'Carbon-13 NMR characterization of the papain adduct formed by peptidyl acyloxy-, aryloxy- and chloromethyl ketone irreversible inhibitors' page 284 ;column 2 ; * abstract and RN [141604-90-2] * & BIOORG. CHEM. vol. 20, no. 1, 1992, pages 42 - 54 -----	1,2	A61K31/16 A61K31/325 A61K31/34 A61K31/35 A61K31/36 A61K31/38 A61K31/44
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 08 OCTOBER 1992	Examiner PAISDOR B.
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons * : member of the same patent family, corresponding document</p>			